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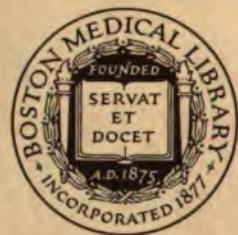
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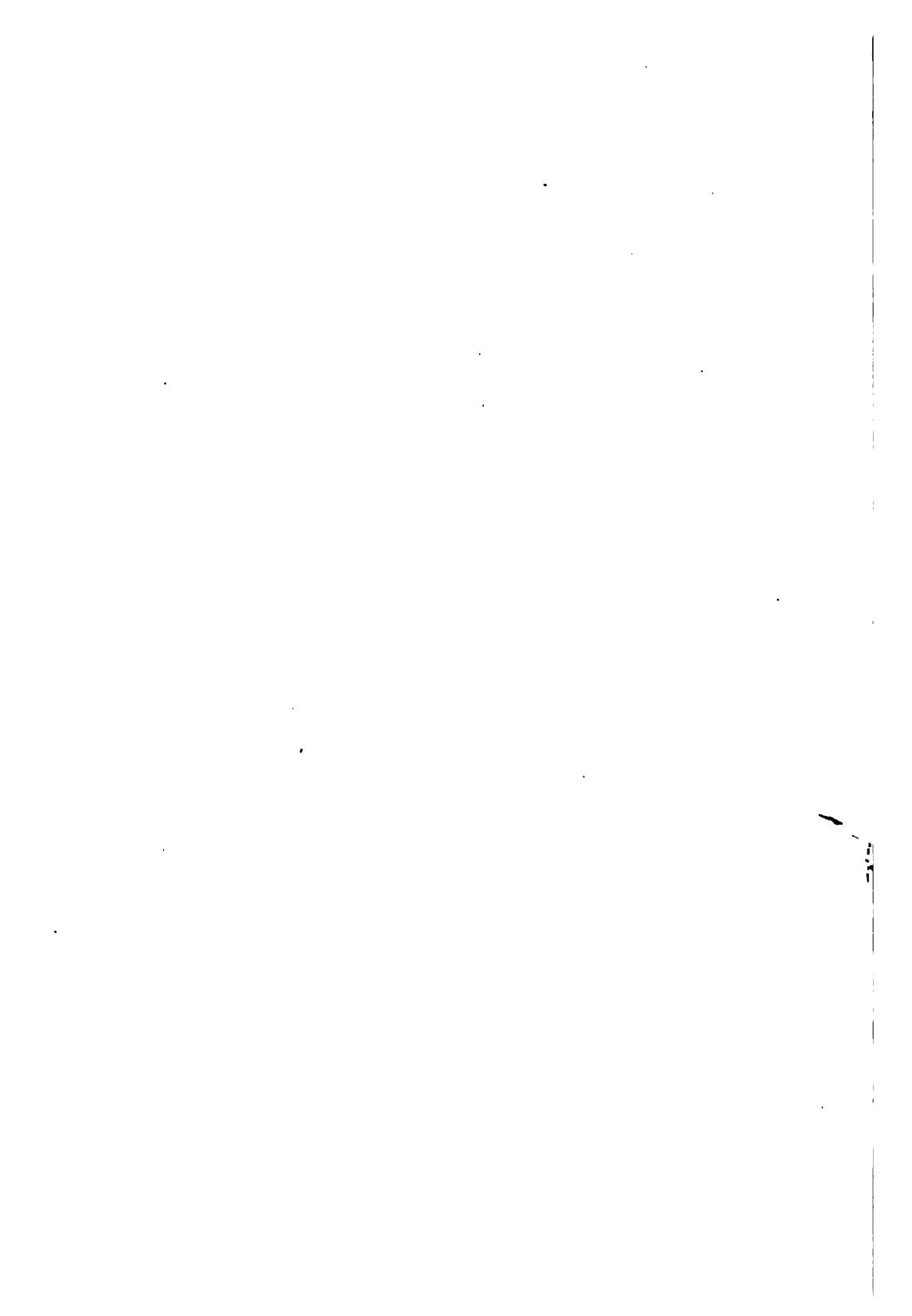


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**Medical and Surgical**

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ANATOMY, PHYSIOLOGY AND BAC

W. A. J.



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# International Medical and Surgical Survey

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**No. 1**

**SECTION 1. ANATOMY, PHYSIOLOGY AND  
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No. 1

**SECTION 1. ANATOMY, PHYSIOLOGY AND  
BACTERIOLOGY**

**1a. ANATOMY AND PHYSIOLOGY**

(1a-1)

(1a-1)

**The Java-Trinil Discovery, "Pithecanthropos."**

*Martin Ramström, Upsala Läkaref. Förh., 36: No. 29, Stockholm,  
Sept. 1, 1921.*

Among the many anthropologic discoveries of the past century, there are 2 which have attracted the interest not only of scientists but also of the general public. One of these discoveries is called "eoanthropos," and the other "pithecanthropos." The scientists who discovered these remains assert that they represent the transition stage between apes and man. The "eoanthropos" remains consisted of human cranial bones and a fragment of an inferior maxilla which resembled that of an ape. It has been maintained that in the evolution of man, the brain and cranium were first affected and that the discovery thus confirms the theory of evolution. The pithecanthropos remains consisted of a cranium which resembled that of apes, and a human femur. The bones were found at points about 15 meters apart, and the discoverers claimed that they belonged to the same individual. The author has studied the various data concerning these discoveries and has come to the conclusion that they do not prove the correctness of Darwin's theory. He criticizes the tendency of anthropologists to reconstruct extremely incomplete fossils, each in accordance with his own anthropogenetic hypothesis. The reconstructions are then sent to museums and described as an evidence of the particular theory at issue. After a few years another anthropologist may reconstruct the results of another discovery, which may be in direct contrast to other previous reconstructions, as his own hypothesis concerning the anthropogenesis is different from those of his predecessors. The theory of evolution can be proved only when more complete fossils are found, especially if the fossils are found in the Orient. The results of the author's studies indicate that the original birthplace of the Aurignac man is to be found in the Orient.

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(1a-2)

(1a-2)

**Possible Relations of the Weight of the Lungs and Other Organs to Body-Weight and Surface Area (in Dogs).**

*G. N. Stewart, Am. J. Physiol., 58:45, Nov. 1, 1921.*

The author states that the observations recorded in this paper were made primarily with the idea that the weight of the lungs, particularly of the blood-free lungs, might be roughly proportional to their average vascular capacity, since the thin pulmonary membrane is largely covered with capillaries.

The experimental procedure was as follows: Twelve dogs were selected, their weight varying from 2.7 kilo to 36.7 kilo. The area of the skin was measured approximately, the animals etherized and then bled to death from the carotids. The skin of the animals was removed, trimmed to a rectangular form, and the area measured. The weights of the animals, free from gastro-intestinal contents, were also obtained.

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The bleeding was exhaustive, but no anticoagulant was employed and there was no washing out with salt solution. The organs were weighed after being dried with a towel. The heart was opened and the interior wiped clean and the same procedure followed for the stomach and intestines. The bronchi were cut off the lungs as far into the lobes as was practicable without removing the parenchyma. The great vessels were cut close to the heart, but subpericardial fat was not removed. The esophagus and rectum were not included in weighing the stomach and intestines. The tabulated results show that, in general, the lung weights are more nearly proportional to skin area than to body-weight. The number of grams of lung per kilo of body-weight increases in passing from the larger to the smaller animals. This also holds for the liver, the kidneys and the stomach and intestines. The spleen weight is much more nearly proportional to the body-weight than to the surface. For the heart, the relation to body-weight seems to be closer than to surface.

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(1a—3)

**Direct Continuity Between Thyroid, Parathyroids and Thymic Nodules in Mammals.**

*A. Dustin and P. Gérard, Compt. rend. Soc. de biol., 85:876, Paris, Nov. 12, 1921.*

Cats, six months of age, were studied. The authors found direct continuity between the parathyroids and a nodule of thymic tissue; the internal parathyroid and the thyroid were directly continuous; thymic and thyroid tissue were directly continuous. This condition has been heretofore reported only in reptiles. The influence of season or age upon the condition is not yet ascertained.

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(1a—4)

**Cytologic Notes on the Hypophysis.**

*H. De Winiwarter, Compt. rend. Soc. de biol., 85:871, Paris, Nov. 12, 1921.*

A series of hypophyses was studied in cats, from birth to the age of six weeks. The volume is doubled during this time and the increase results almost entirely from growth of the nervous portion. The glandular portion is composed of two kinds of cells, chromophobes and chromophiles. He did not find the so-called transition forms, and does not agree with most physiologists as to the function of these cells. He thinks they are protecting rather than secreting cells, but this must be verified by physiological studies. Large, elongated cells, which have not been discovered before, also occur in the anterior lobe. They are really degenerating cells and leave lacunae when they are absorbed. They probably represent merely a transitory phase of development. The histologic appearances are described in detail with illustrations.

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(1a—5)

**Anatomy of the Thymus of the Rabbit, According to Age.**

*Erik Gedda, Upsala Läkaref. Förh., 36: No. 9, Stockholm, Sept. 1, 1921.*

The author has performed several experiments on rabbits for the purpose of determining the quantitative relation of the cortex, medulla and the interstitial tissue. The cortex-medulla index was also de-  
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(1a—5)

terminated. The experiments were performed on 120 rabbits, which were grouped in 12 different age groups. The results were compared with those of other authors, and the following results were obtained: The experiments showed that, although the parenchymatous and the adipose tissues from which the thymus is composed at the time of involution are very labile, they are not dependent upon the same factor, as regards their quantitative relation to each other. Under normal conditions the adipose tissue seemingly plays a more important rôle than does the parenchymatous tissue. The determination of the index showed that in the age-involution of the thymus of the rabbit the involutorial change of the cortex is not greater than that of the medulla. This condition in the rabbit differs from that in human organs, and depends upon the more important rôle which the lymphocytes play in the organism of the rabbit, throughout the entire life of the animal. The changes in the number of leukocytes in the thymus is therefore not dependent upon any local causes, but is regulated by the general number of the lymphocytes in the organism of the rabbit.

The series of experiments are not complete, and this is only a preliminary report. Numerous tables are included in the article, illustrating the results of the examinations.

(1a—6)

**The Development of the Pharynx and Aortic Arches of the Turtle, with a Note on the Fifth and Pulmonary Arches of Mammals.**

*Ralph Faust Shaner, Am. J. Anat., 29:407, Nov. 15, 1921.*

The pharynx of the turtle produces 5 pouches and a postbranchial body. The first 4 are ordinary lateral outgrowths of the entoderm. The first pouch becomes the auditory tube and the lining of the tympanic-mastoid cavity. The second disappears. The third produces dorsal and ventral outgrowths which become, in the adult, the anterior thymus and the anterior parathyroid gland, respectively. From the fourth pouch, in the same manner, are developed a dorsal posterior thymus and a ventral posterior parathyroid gland. The fifth pouch atrophies. Behind the fourth pouch, in the angle between it and the pharynx, there develops a diverticulum which is clearly a postbranchial body from which a true fifth pouch develops. The postbranchial body is not a pouch for a pouch develops from it; it never has those relations to nerves, branchial placodes, and aortic arches which characterize a true pouch. Neither is the postbranchial body an outgrowth of a pouch, in the sense that the thymus and parathyroid glands are, for it grows out directly from the pharyngeal wall and precedes the fifth pouch, the only one from which it could be derived. The true pouch derivatives do not appear until much later, and when they do, the postbranchial body is not in series with them. The author believes the postbranchial body is better considered as a caudal prolongation of the pouch-forming area—a remnant out of which the fifth pouch develops and from which a sixth would spring, if such were to appear.

**Aortic Arches.** These are 6 in number and they appear serially from before backward. The first 2 are transient vessels, the third persists as the internal carotid artery, and the fourth as the systemic aortic arch. The fifth appears soon after the fourth is completed and becomes a fully developed arch. The sixth arch begins as a bud from

the fifth, springing from the latter above the fifth pouch and running ventrally behind the fifth pouch and lateral to the postbranchial body. In the 6.6 mm. embryo, the arch ends blindly; in an older embryo of 8.4 mm., it rejoins the fifth below the pouch and becomes a complete functioning vessel. The sixth arch thus constituted, differs from the preceding ones in beginning and ending in the arch anterior to it. For some time the proximal and distal parts of the fifth arch serve as common trunks for the fifth and sixth arches. On the degeneration of the fifth arch, the sixth takes over its proximal and distal parts to form the composite pulmonary arch. Because the mammalian fifth arch, so-called, is more closely related to the fourth and appears after the pulmonary arch, the author follows Lewis in considering the fifth arch of mammals to be an atypical vessel, though presumably a true arch. Moreover, since the mammalian pulmonary arch lies medial to the postbranchial body and takes the course not of the reptilian sixth arch, but of a transient irregular vessel found in some turtle embryos, it cannot be strictly correlated with the sixth arch of lower vertebrates.

(1a-7)

(1a-7)

**Genesis of Papillas of the Human Tongue.**

*Torsten J:son Hellman, Upsala Läkaref. Förh., 36: No. 11, Stockholm, Sept. 1, 1921.*

The author has studied the genesis of the various papillas of the tongue and, as he had at his disposal the very extensive embryologic material of the Anatomical Institute of Upsala University, believes that he has obtained a complete insight into the question. He examined 43 embryos of various sizes. As the nerve-stems are very distinctly developed, even in the earlier stages of fetal development, it was very easy to follow the nerves and even their branches in the sections, and all possible mistakes could be avoided. The anlage of vallate papillas is observed in earlier stages of fetal development than has hitherto been thought to be the case. It appears even in embryos from 20 to 40 mm. in length. The branches of the glossopharyngeal nerve grow toward the epithelium and, having come in contact with it, they form bud-shaped formations expanding the epithelium. The nerve-buds penetrate further into this tissue, the buds becoming larger. They are finally separated from the nerve branches by a neck, and form oval or round papillas. A primary formation with a secondary division of the papillas by the epithelial growth—as was earlier thought to be the case—does not exist. The vallate papillas develop from the beginning as protrusions of the epithelium due to pressure of the branches of the glossopharyngeal nerve and maintain their local character. The epithelial growth has nothing to do with the primary formation of papillas, but is merely a secondary phenomenon in the later stage of their development. The taste-bud anlage of the vallate papillas also appears very early and could be observed in an embryo 18.7 mm. in length.

The anlage of the foliate papilla could be observed in embryos 30 mm. long, and consisted in a formation of depressions of the epithelium in the stratum proprium. The anlage is inconstant in embryos between 30 and 70 mm. long. The branches of the glossopharyngeal nerve divide and radiate toward the region of origin of the papillas. In only 2 cases of embryos in a later stage of development, could rudiments of taste-buds be observed. The examinations showed the foliate papilla to be rudimentary.

The anlage of the fungiform papilla was also observed in an early stage of fetal development, that is, before the embryo was 20 mm. long. The author believes that the glossopharyngeal nerve pushes the taste-bud, together with the surrounding epithelial cells, before it until the surface of the tongue epithelium is reached and thus a fungiform papilla is formed. The epithelium is first connected with the nerve, but the formation of connective tissues between the epithelium and the nerve separates the nerve from the epithelium and the papilla becomes gradually hemispheric or conical. The epithelial growth around the basal part of the papilla then completes the development of the papilla by forming a groove.

The filiform papillas are formed by the growth of small connective tissue papillas toward the epithelium, in embryos 45 mm. long. Only when the embryo is 70 mm. long, do these papillas form small depressions on the surface of the epithelium. There are such great histogenetic differences in the development of the various forms of papillas that the author does not consider it possible that one papillary form can change to another. The formation of double vallate papillas probably depends upon a double anlage or branching of the nerve-stem, which is observed in the early stage of fetal development. Numerous illustrations are included.

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(1a—8)

**Phylogenesis of the Gall-Bladder.**

*Ivar Broman, Upsala Läkaref. Förh., 36: No. 7, Stockholm, Sept. 1, 1921.*

(1a—8)

The origin and function of the gall-bladder are mysterious. The liver cells secrete bile permanently and when the bile cannot be carried off by the intestinal canal, it collects in the gall-bladder. It has, however, been observed that in certain animals, such as rats, horses and pigeons, no gall-bladder develops under normal conditions, although it cannot be presumed that the function of the liver cells and the mechanism of the hepatopancreatic duct in these animals is different from that of other closely related animals with gall-bladders. It has also been proved that the gall-bladder may be extirpated without any injury or secondary changes in the biliary duct. Furthermore, the function of the gall-bladder is of very little importance. The author considers it a very remarkable fact that such great topographic and morphologic differences exist in the gall-bladders of various vertebrates that Gegenbauer considered that they could not be homologous formations. Other older authors considered the gall-bladder to be only "a modified biliary duct." This hypothesis would easily explain the great differences in the development and function of the gall-bladder in different animals, and would also explain satisfactorily the absence of the gall-bladder in certain animals. If, however, this hypothesis were correct, the gall-bladder would appear comparatively late in the ontogenesis; its function would also be comparatively important. However, this is not in accordance with the facts.

On the basis of his studies, the author believes that the gall-bladder is nothing but a rudimentary organ, and should be considered only as a rudimentary part of the liver. He bases his theory upon the following facts: It is generally thought that the gall-bladder develops from the caudal part of the first hepatic rudiment; the caudal part of the liver is

therefore called the pars cystica. This first rudiment of the functionally insignificant gall-bladder may develop simultaneously with the functionally very important hepatic rudiment and may be very large in its early stage of development. In some of the vertebrate animals the gall-bladder is connected with the liver by means of connective tissues but in others it is totally separate from the liver—as, for instance, in man. In certain animals, again, it is very slightly connected with the liver. The author believes that his theory could easily be proved by means of animal experiments and he considers mice and rats to be the best for such experiments.

(1a—9)

(1a—9)

**Reconstructed Models to Illustrate the Development of Biliary Capillaries in Rabbits.**

*Carl Löwenhjelm, Upsala Läkaref. Förh., 36: No. 21, Stockholm,  
Sept. 1, 1921.*

From a few reconstructed models of the livers of young and adult rabbits, the author has observed that the majority of the liver-cells turned three surfaces toward the blood-capillaries and three surfaces toward the other liver-cells. In the center of the contact surface between the liver-cells are the biliary capillaries, which meet in a point on the surface of the liver-cells. According to Hering, 4 such biliary capillaries meet at the point of junction, but the author observed only 3 converging capillaries. This form of liver-cell was the most frequently found, but other forms were also observed. On the periphery of the lobule were found cells which were bordered on only two sides by biliary capillaries. These cells were more frequent in the neighborhood of the central vein, in which the capillary anastomoses were closer together and the cells were less closely associated. In another variation, the capillaries were bordered only by two liver-cells. There were also accessory capillaries which ran between two cells in the direction of the vascular lumen, and had blind endings.

During the embryonic period the liver serves as a blood-forming organ. Its definite structure is rendered more important not only by its function as a sac in which are found the blood-forming cells which are furnishing material for the new capillaries, but also by the fact that when the blood-forming cells disappear after a few days, a decrease of the volume of the liver results; the relation of the liver-cells toward each other is also modified, so that the accessory capillaries of the biliary vessels meet and form a cytozoic net-work.

(1a—10)

(1a—10)

**The Regressive and Retention Phenomena of the Embryonic Human Kidney.**

*Carl Sundberg, Upsala Läkaref. Förh., 36: No. 30, Stockholm,  
Sept. 1, 1921.*

The author has studied the regressive and retention phenomena of the embryonic human kidney. The length of the embryos varied between 18 and 65 mm. The wax models from these embryos showed surprisingly regular and numerous regressive and retention phenomena. The conformity of the findings in all the kidneys and the absence of pathologic conditions in the embryos proved that the phenomena were due to physiologic factors. In 4 embryos, rudiments of Bowman's cap-  
(Sec. 1—Page 6)

sules and secretory tufts (pseudoglomeruli) were found associated and fused with collecting tubules of a secondary stage. In the literature the earliest appearance of rudiments of Bowman's capsules and of secretory tubules is described as occurring in association with collecting tubules of the fifth stage. The author also observed that the first appearance of the metanephrogenic capsules does not occur in the form of cysts or balls, but in the form of thin disks. The disks have a diameter of 80  $\mu$ . and are 20  $\mu$ . thick. The first regressive and retention phenomena occur in a very early stage of embryonic development. The phenomena are much more frequent than is generally thought, and include at least all early rudimentary stages. Best's carmin method is especially suited for the staining of the epithelium of the urinary passages, to differentiate it from the secretory epithelium, and for the staining of young embryos.

(1a—11)

Studies in the Dynamics of Histogenesis. Tension of Differential Growth as a Stimulus to Myogenesis. VIII. The Experimental Transformation of the Smooth Bladder Muscle of the Dog, Histologically, into Cross-Striated Muscle, and Physiologically, into an Organ Manifesting Rhythmicity.

Eben J. Carey, *Am. J. Physiol.*, 58:182, Nov. 1, 1921.

Experiments were undertaken to prove that, so far as muscular tissue is concerned, function determines structure. The bladder of a young dog was used because it possesses the smooth, pale type of muscle. An attempt was made to transform the vesicular non-striated muscle into cross-striated muscle, by varying the velocity of application and the intensity of the tensional stimulus to a higher optimum degree. The procedure was as follows: Through a silver suprapubic tube transfixed into the bladder of a 4 weeks old dog, concentrated boric acid at 37.5° C. was passed from a reservoir, under varying volume and pressure conditions and at various intervals of time daily. The volume of boric acid passed by the bladder gradually increased. The urethral passage of urine became of the nature of clonic, short, rapidly recurring contractions, but later the clonic nature of the bladder contractions was lost and a greater volume of fluid was passed with each urethral relaxation. Corresponding to each individual contraction of the bladder, a complete urethral relaxation occurred. By reducing the volume and pressure of the fluid circulating through the bladder the vesicular contractions are retarded; by complete inhibition of the circulation no contractions are elicited. The stimulus that causes the rhythmic beat of the bladder is hydrogenic in nature. The rhythmic beat is dependent also on the irritability of the responding mechanism. The structure of these pressure curves is illustrated by photographs of tracings obtained on a recording drum.

The experiment began March 29. Prior to this date the dog passed an average of 250 c.c. of urine in 24 hours. May 20 to 21 this same bladder passed the enormous volume of 50,000 c.c. boric acid during ten hours of experimental observation. The excised portion of the bladder, taken when the experiment began, was normal smooth muscle of a developing bladder. The portion taken May 21 showed definite cross-striations and an increase in width and length of the muscle fibers over that of the control animal. The author remarks that the different

degrees of energy possessed by the vesicular smooth and cross-striated muscles here studied is purely a biomechanical problem, corresponding to the differential amount of work that has been expended in their formation. It was also found that the transition epithelium of the bladder had undergone hyperplasia and appeared as stratified squamous epithelium. The vesicular epithelium showed 10-30 layers. The inner group of cells was greatly flattened and elongated; in certain locations no nuclei were seen in the layer bounding the lumen. In the greater part of the epithelium of the bladder, the cells were nucleated from the basal to the inner group of cells.

The essential difference between the pale smooth muscle of the bladder and the red involuntary striated muscle of the heart depends upon the differential intensity of hydrodynamic tensional stimuli to which the vesicular and cardiac mesenchymal cells, respectively, have been subjected during development. The structure of muscle is determined by the function it performs and the work it does. Cross-striated muscle is not formed in anticipation of a future function. The conclusion is warranted that function, in this case, determines structure, and not the reverse.

(1a—12)

**Origin of the Sympathetic Nervous System in Amphibia.**

*Erik Müller and Sven Ingvar, Upsala Läkaref. Förh., 36: No. 23, Stockholm, Sept. 1, 1921.*

The ventral and dorsal roots of the spinal nerves of amphibia and higher species of vertebrate animals are joined together so early in the course of development and so closely that it is impossible to separate them. It is, therefore, impossible to determine whether or not the ganglion which later develops from these nerve roots originates in the anterior or in the posterior part of the root. It is necessary to change the developmental process of the ganglion in order to be able to determine the origin of the ganglion. Kuntz and Batson have recently reported such experiments. They destroyed the ganglion ridges by electrolysis, and obtained embryos in which the spinal ganglion and the dorsal nerve-roots were lacking, while the sympathetic ganglion developed normally. The authors believe that the results of Kuntz's and Banton's experiments confirm the theory that the sympathetic ganglion originates in the medullary cells which move along the ventral nerve-root.

The authors have also performed similar experiments on *Rana temporaria* for the purpose of studying the origin of the sympathetic nervous system in amphibia. They observed that when the spinal ganglion was totally removed the sympathetic nervous system of the animals was totally lacking. In animals in which the dorsal part of the spinal cord was removed, the spinal ganglion was usually lacking while the ventral nerve-roots developed normally and were entirely free from Schwann cells. It was also observed that the medullary cells advanced into the ventral nerve-root. The authors do not believe that this movement on the part of the cells has any influence whatever on the development either of Schwann's or of the sympathetic cells. In animals in which a ventral operation was performed no ventral nerve-roots were found, but the spinal ganglion developed normally and continued in the form of cellular branches in the space between the chorda and the myomere.

On the basis of the results of these experiments, the authors are convinced that the sympathetic ganglion of anamniotic animals originates in the spinal ganglion.

(1a—13)

Inquiries Concerning the Number of Cells in the Human Cerebral Cortex.

Hans Berger, *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 69:46, Berlin, July 30, 1921.

Ramon y Cajal first pointed out that the degree of differentiation of cerebral ganglion cells can be determined by their distance from each other, since the interstices between them are occupied by nervous and protoplasmic ramifications. Berger, whose experiments confirmed this view, conceived the idea of comparing corresponding areas of the two cortical hemispheres of the same human brain. It is necessary to choose areas of known function, for instance, the motor regions, and more especially the hand centers, which have been explored by Lippmann, Horsley, Krause, Brodmann.

By Hammarberg's method the respective portions of the anterior central convolutions are hardened in alcohol and embedded in paraffin, and cut into 5 serial sections 20 microns thick. In these sections, stained with thionin, a cell-count is made, always of 0.01 sq. mm., in a strip 0.1 mm. wide throughout the thickness of the cortex. These counts are made at the apex of the convolutions and as far as possible at the same point in the 5 serial sections. By averaging the figures obtained for 0.01 sq. mm. at the various depths of the cortex in 5 serial sections, the number of cells in each 0.001 cu. mm. of the cortex is ascertained. The author's counts of cells in the right and left hemispheres at depths from 0.1 to 2.8 mm. are tabulated.

The first application of this method in examining the brain of an intellectual lady, dying of heart-disease at the age of 39 years, produced striking results. At a depth of 0.3 mm. the cell-count was 68 for the left and 99 for the right hemisphere. But in two other persons—one an assessor, dying of pneumonia at 26, and the other a servant-girl, dying of heart-disease at 23—an examination under improved conditions produced negative results, so that it was concluded that any histologic differences between the two hemispheres cannot be ascertained by this method.

Berger then sought to determine whether the method might serve to ascertain the progressive differentiation of specified areas during the years of development. In the brain of a girl, dying of pneumonia at 11 years, he counted 72 cells in the left and 42 in the right hemisphere at a cortical depth of 0.4 mm. But as close examination revealed that the difference was caused by the variability of cerebral fissures and convolutions, further application of this method for such comparison was discontinued.

The cell-counts did yield one interesting collateral result on a different problem, namely, the size of the entire cortical mass of the human brain. By a modification of Anton's method, photographs were made of the sections. The cortical and medullar portions were then carefully cut out and, by weighing, their surface area was determined. This method was applied to two cases: (1) A boy dying of tuberculosis at 10 years; weight of brain 1,104 gm., and of cerebrum 962 gm.; cor-  
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tical mass 439.919 c.c., white mass 321.541 c.c., ratio 100:73. (2) A man, 36 years old, dying of pneumonia, weight of brain 1,245 gm., and of cerebrum 1,090 gm.; cortical mass 529.726 c.c., white mass 397.543 c.c.; ratio 100:75. These figures fairly agree with the results of Henneberg and Jäger, who computed the cortical mass of the adult brain as 540 and 539 c.c., respectively. It may be said that, between the tenth year and adult age, the cortical mass increases by 90 c.c. and the brain weight by 141 gm.

In conclusion, Berger computes the number of ganglion cells in the entire cortex, on the assumption that the mass is about 540 c.c., as 5,512,-000,000, which lies midway between the figures obtained by Meynert (1,200,000,000) and by Thompson and Donaldson, as quoted by Ziehen (9,200,000,000).

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(1a—14)

**A New Method of Staining Neuroglia-Fibers.**

*W. Holzer, Ztschr. f. d. ges. Neurol. u. Psychiat., 69:354, Berlin, July 30, 1921.*

In this new staining method, which is based on a combination of Weigert's and Mallory's methods and the successful application of which is illustrated by a series of very clear photographs, the technic is as follows:

(1) Mix equal parts of an aqueous 1% phosphomolybdic solution and alcohol (absolute or 96%); then add 2 drops of concentrated acetic acid for each 20 c.c. of the mixture. (This mixture does not keep for more than a few days.)

(2) Immerse the frozen formol sections in this mixture for 1-2 minutes. Then lift them out on the slide and remove the superfluous liquid; the sections should lie flat and remain moist. (The following operations must be carried out rapidly, occupying not more than 5 minutes.)

(3) Blot the sections with filter paper soaked with a mixture of absolute alcohol (2 parts) and pure chloroform (8 parts) so that they are well moistened with the liquid.

(4) Pour on a few drops of the staining fluid composed of absolute alcohol (2 c.c.), chloroform (8 c.c.), and crystal violet (0.5 gm.).

(5) Pour on the bromid solution (potassium bromid, 10%, with 5 drops of 1% solution of sodium hydroxid) until the greenish-metallic film forming on the surface disappears.

(6) Blot the surface of the sections with filter paper and then pour on the differential stain, freshly made of anilin, 4 c.c.; chloroform, 6 c.c., and 4 drops of 5% solution of sodium hydroxid, and filtered.

(7) Rinse with xylol and finish with xylol Canada balsam.

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**Evolution of the Adult Ovary of the Female Rabbit.**

*A.-L. Salazar, Compt. rend. Soc. de biol., 85:783, Paris, Oct. 29, 1921.*

Previous statements of the author have been somewhat misunderstood; supplementary comment is therefore made. Complete evolution of the ovary of the female rabbit, including senile changes, has not been studied. Bibliography is scattered and uncertain. Present observations (Sec. 1—Page 10)

of the author must be received with some reservation. It is unknown whether ovarian evolution is spontaneous, as determined by endocrine secretion, or due to coitus; in the first case, the corpus luteum would be an evolutionary organ; in the second, it would not, and may therefore be temporarily disregarded. The adult ovary of the rabbit is of 4 types, ovigenous, follicular, atresic and interstitial. The ovigenous cords of the ovigenous type of ovary have nothing in common with the cords of Pflüger. The histology of each type is described. The logical sequence would be ovigenous, follicular, atresic, reticulated interstitial, non-reticulated interstitial. The interstitial type occurs in long and heavy animals; the atresic and follicular types occur in animals of medium weight; the ovigenous type is noted in the lighter and smaller animals. The only doubtful point is the numerical order of proliferation of the ovigenous types. It would seem to occur at the beginning of adult life. In any reports, the type of ovary studied should be recorded.

(1a-16)

**Maturation and Experimental Activation of the Ovum in Sabellaria.**

*E. Fauré-Fremiet, Compt. rend. Soc. de biol., 85:810, Paris, Nov. 5, 1921.*

Maturation of the ova of *Sabellaria alveolata* and *S. spinulosa* is described. The author has endeavored to discover simple conditions which prevent maturation when the ovum is in contact with sea-water. Oxygen has no influence. Increased concentration of salt (sea-water plus sodium or magnesium chlorid), merely retards the formation of the primary spindle. Neutralized or slightly acidified sea-water prevents the transformation of the germinal vesicle and the appearance of the spindle. The requisite quantity of acid is such that the water is still alkaline to methyl orange while very slightly acid to neutral red. Female *Sabellaria* have a freezing-point from 0.6° to 0.9° C. below that of the surrounding sea-water. Maternal tissues, especially about the eggs, are much less alkaline than sea-water. At the moment of deposition, the ovum enters a medium of stronger alkalinity and weaker osmotic pressure than the maternal medium, the new conditions being necessary and sufficient to initiate mitosis, but only as far as the metaphase. Further studies have shown that the determination of maturation and of artificial activation of the ova of *Sabellaria* correspond to results obtained by Loeb for various other genera. Ova of *Sabellaria* are easily obtained; studies have been made at the marine biological laboratory at Croisic, administered by the medical school at Nantes.

(1a-17)

**Morphological and Physiological Studies on the Musculature of the Mature Graafian Follicle of the Sow.**

*M. S. Guttmacher and A. F. Guttmacher, Bull. Johns Hopkins Hosp., 32:394, Dec., 1921.*

Previous accounts of the existence of smooth muscle fibers in the walls of the Graafian follicle have been confirmed. In the pig these muscle fibers form a considerable portion of the theca externa. The sympathetic nerves, long known to run to the neighborhood of the follicles were traced to a direct connection with the muscle fibers, and finally the contraction and innervation of the musculature was studied

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by selective chemical stimulation, applied to isolated strips of the follicle wall maintained at body temperature in oxygenated Locke's solution. Since the musculature is contracted by the action of physostigmin and relaxed by epinephrin and atropin, its innervation is considered similar to that of the intestine, with nerve fibers from the parasympathetic system carrying relaxor stimuli. This neuromuscular apparatus is conjectured to serve the purpose of rupturing the mature follicle, but definite proof of this hypothesis has not as yet been secured.

(1a—18)

**Imperfect Karyokinesis of Artificial Cells.**

*Herrera, Gac. méd. catalana, 59:99, Barcelona, Aug. 31, 1921.*

The compressed fluorosilicic cells prepared from a solution of sodium silicate and potassium difluorid portray important aspects of karyokinesis. The technic is complicated and requires skill and care for the successful performance of the various cytologic manipulations necessary to the reproduction of the karyokinetic activities in artificial cells. The cells are stained with ferric hematoxylin, dried with alcohol and mounted in balsam. In the center of the cells are seen vesicles and spindles with filaments of chromosome in the equator of the spindles. There are frequently two longitudinal segments which circumscribe an empty elliptical space. In the superior and inferior extremities of the spindles are vaguely seen pseudoasters. In some of the cells filaments are rolled up in a vesicle or nucleus. Doubtless because of defective technic karyokinesis does not occur completely and the divisions which take place are limited to the first stage, which generally is direct, and to the second, which is indirect and subject to many variations and irregularities difficult to explain.

(1a—18)

(1a—19)

**Measurement of Mitotic Angles in Various Lymphoid Cells.**

*V. Ellermann, Compt. rend. Soc. de biol., 85:751, Oct. 22, 1921.*

The extent of the apical angle of the mitotic spindle is important as a means of differentiating not only cellular elements, but varieties of mitosis. Measurements were made with a goniometric ocular of at least 40 angles occurring with each variety of mitosis. The mean figures were as follows: First group: megaloblasts, 18°; erythrogonia (hematoblasts), 21°. Second group: leukemic lymphoblasts, 38° to 42°; normal lymphoblasts, 39°. Third group: neutrophils, 66°; eosinophils, 73°. Fourth group: chronic leukemic myeloblasts, 68°; acute leukemic myeloblasts, 69°. The author thinks the method differential for erythrogonia and myeloblasts. The mitotic angle within the several groups has the following range; erythrogonia, 2° to 40°; lymphoblasts, 6° to 74°; myeloblasts, 32° to 106°. Mathematic derivations for a given number of angles, with variable ranges, are given.

(1a—19)

(1a—20)

**Age and Multiplication of Fibroblasts.**

*Alexis Carrel and Albert H. Ebeling, J. Exper. Med., 34:599, Dec. 1, 1921.*

Pure cultures of fibroblasts were grown on the plasma of young, middle aged, and old chickens. It was found that the rate of growth, as shown by the width of the ring of connective tissue produced around

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the fragments, varied in inverse ratio to the age of the animal from which the plasma was taken. The differences were great, growth being much more rapid where plasma from young animals was used. The duration of life of the fibroblasts also varied inversely with the age of animal from which the plasma was taken. The sera of 20 and 45 year old human beings exhibited the same phenomena when used as media. An attempt was made to determine whether this difference was due to a loss of a growth-accelerating substance present in the serum of the younger individuals or to the development of an inhibiting one in the older. A comparative study of media containing varying amounts of sera showed that high and low concentrations of the serum of young individuals did not influence the rate of multiplication of the fibroblasts, while a high concentration of serum obtained from an old animal had a markedly depressing effect on the growth. The action of age is therefore not due to the decrease of an accelerating factor but to the development of a growth-inhibiting factor in the serum.

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(1a—21)

**Nuclear Staining in Over-Fixed Specimens.**

*M. Fabre and J. Devuns, Compt. rend. Soc. de biol., 85:858, Paris, Nov. 12, 1921.*

Keeping specimens for more than twenty-four hours in chromate fixatives interferes with staining, especially of nuclei. The authors suggest the following method of counteracting overfixation: Sections already cemented to the slide may be plunged into a strong solution of sodium bicarbonate; even a saturated solution may be used. For tissues fixed and imbedded, paraffin is removed by xylol or toluene; the sections are passed through absolute alcohol, 90% alcohol, collodion, 70% alcohol, and, for from five to ten minutes, 10% sodium bicarbonate. They are then carefully washed and stained.

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(1a—22)

**Uranium Nitrate for Fixing Mitochondria.**

*A. Tupa, Compt. rend. Soc. de biol., 85:848, Paris, Nov. 12, 1921.*

The author has found 40% formaldehyd unsatisfactory, except for hepatic mitochondria. Uranium nitrate may be substituted for potassium bichromate, or, preferably, combined with it. Mitochondria of the liver, kidney, gastric mucosa, spinal cord and eye-ball, in rabbits, rats and guinea-pigs, have been studied, by means of 2 solutions: (1) commercial, 20% formol, 100 parts, uranium nitrate, 1 part; (2) Regaud's solution IV, 100 parts, uranium nitrate, 1 part. The pieces of tissue should be small; trauma should be carefully avoided in removing them. The duration of fixation should be from eighteen to twenty-four hours, not over forty-eight hours. After from eight to ten hours, the bichromate-formol-uranium solution should be renewed; it soon becomes dark, but not turbid. After-treatment with bichromate is useless. The fixed tissue-blocks are washed in running water for from two to twenty-four hours, dehydrated and imbedded in paraffin. The zone which is suitable for sectioning is covered by a layer about 150  $\mu$ . thick, which is useless because of immediate exposure to the fixative. Beneath this layer, there is a layer about 200 to 300  $\mu$ . thick, which is suitable for study. Then follows a layer of poor fixation. Sections, 2.5  $\mu$ . thick, are stained with iron hematoxylin. Frozen sec-

tions, from 4 to 5  $\mu$ . thick, may be stained by the rapid, hot method with iron hematoxylin. The author considers uranium nitrate important for the preservation of mitochondria in nervous cells, which are very difficult to fix. The advantages of the method are the precision and constancy of fixation, the solidity of the mitochondria stained in this way, the simplicity and the rapidity of the method, due to the elimination of the after-use of bichromate. The appearance of mitochondria stained by different methods is described in detail.

(1a-23)

**Studies on Endothelial Reactions. V. The Endothelium in the Healing of Aseptic Wounds in the Omentum of Rabbits.**

*Nathan, Chandler Foot, J. Exper. Med., 34:625, Dec. 1, 1921.*

The small mononuclear endothelial cells—endotheliocytes, are vitally stained *in situ*, by the intravenous injection of colloidal carbon. A 50% mixture of Higgins' waterproof drawing ink and distilled water is used for this purpose. This is the only reliable means, for the more diffusible colloidal stains also stain cells that were never part of the endothelium. In a series of rabbits aseptic wounds of the omentum were produced by through and through silk sutures. The lesions were studied at different intervals covering periods from two hours to five weeks. The proliferation of the capillary endothelium resulted in the production of: (a) new vessels, (b) phagocytic endotheliocytes, and (c) cells which are indistinguishable from fibroblasts. The three types appear to be freely interchangeable. Collagen fibers are formed, apparently independently of cellular activity, from fibrin or some substance associated with fibrinous clots. Wound healing does not seem to take place, as described in some text-books, by an orderly progression of specific cells to designated positions. The surface epithelium and the vascular buds alone may act in this way. The mononuclear cells of mesenchymal type appear to wander into the injured area and later react in varying ways. The process of wound healing cannot be fully understood until we know more of the physiology and chemistry of normal mesenchyma.

(1a-24)

**An Attempt at Restoration of Parenchymatous Tissue.**

*Nathan, Capette and Madier, Bull. Acad. de méd., 86:223, Paris, Nov. 1, 1921.*

One of the authors has already reported that bones are made up of a fertile layer (Haversian layer) which is separated from the periosteal connective tissue by an external isolating sheath. If the latter is removed by accident or operation, the Haversian layer proliferates into the connective tissue and produces bone. In order to ascertain whether similar phenomena take place in viscera that are separated from the surrounding loose connective tissue by a dense capsule, experiments were first made on the liver of a rabbit. A deep cut was made in the organ and a portion of the great omentum inserted in the wound. Six weeks later small nodes of migrated hepatic cells were found in the connective tissue. Similar results were observed when the operation was repeated on the kidneys and thyroid. The authors conclude that the dense tissue that surrounds the parenchyma of the liver, kidneys and thyroids prevents their proliferation into the sur-

rounding connective tissue. The new growth is somewhat similar to the proliferation of embryonic epithelium into the mesenchyma. Regeneration is only possible when the parenchyma is sound or still has at least some vitality. Finally the suggestion is made that this method may eventually be applied to the treatment of chronic visceral insufficiencies.

(1a—25)

**Congenital Absence of the Pectoralis Minor and of the Inferior Portion of the Pectoralis Major on One Side.**

*Henri Roger, Marseille-méd., 58:938, Oct. 15, 1921.*

The lower portion of the pectoralis major and the pectoralis minor of the man in question were missing on the left side. The medial end of the right clavicle was specially prominent. No other abnormality of muscles or bones was found. The Wassermann was negative. The father is probably epileptic and has attacks of transitory paralysis or aphasia. One sister has a quadriplegia, probably of myopathic nature. The mother is very nervous.

Seventy similar cases have been reported so far. Some authors consider this condition as a sign of degeneration. Anomalies of both the ribs and overlying muscles have been ascribed to the close application of a fist of the fetus against the thoracic wall during the early months of intrauterine life. It is conceivable that this might likewise explain a purely muscular anomaly. Intrauterine infantile paralysis has also been invoked. The epileptic condition of the father and the myopathy of the sister point in this case to a possible hereditary origin of this abnormality. Syphilis may also be thought of in spite of the negative Wassermann, as the mother of the patient had two miscarriages. The absence of these muscles produced only a slight diminution of strength in the patient.

(1a—26)

**A Case of Hereditary Polydactylism Occurring in Four Generations and Many Members of the Same Family.**

*E. Miles Atkinson, Brit. J. Surg., 9:298, Bristol, Oct., 1921.*

Of 48 persons in four generations 26 exhibited a condition of polydactylism, 17 being males and 6 females. The predominance of males does not hold for all branches of the family, for on one side the deformity was transmitted from a male through a female chiefly to females. There seems to be no mendelian feature or other common factor in its transmission. In all but two cases the identical condition occurred—a supernumerary digit upon the posterior border of each hand and foot. There is no history of more than one extra digit on any one limb in this family. According to Tubby the commonest double digit is the fifth, the next most common being the first. The degree of development varies; often the digits can be flexed and extended but rarely abducted or adducted. In this series the anlage of the metacarpal bones was present in most cases. The work of Howes and Hill on the Dorking fowl shows that accessory digits are due to fission and that any increase or decrease from 5 as a normal phenomenon is to be regarded as specialization. The roentgenograms tend to confirm the theory that accessory digits are due to a process of dichotomy which

if it had extended further, would have produced an accessory limb. Dicephalic infants afford no safe ground for believing that one single head is derived from a primitive condition of polycephaly.

(1a-27)

**An Adult Living Case of Total Phocomelia.**

*H. R. O'Brien and H. S. Mustard, J.A.M.A., 77:1964, Dec. 17, 1921.*

While engaged in the work of rural sanitation of U. S. Public Health Service in northeastern Kentucky in the summer of 1917, the authors saw a man, aged 29, whose extremities were remarkably abbreviated. He was 37½ in. tall when standing on the condyles of the femurs, his weight was about 52 lb., but was increasing. The head was 18½ in. in circumference and apparently normal except for highly arched palate and mouth-breathing habit; the nose was not examined; the tonsils were normal. The right clavicle was broken in 1916. The trunk was fairly normal, though reduced in dimension. There was some lateral curvature of the spine, concavity to the right, especially noticeable from the rear. The heart was normal to palpation. The abdomen was strangely rigid and tense. The external genitals were normal, the left testicle being slightly larger. He had had nocturnal emissions since age 13. His mother stated that the foreskin was absent since birth, as was the case with two other monster children. The arms were alike, the left being a little longer and larger, 8 in. from tip of finger to shoulder. Some movement was possible at the joints, greatest at the shoulders. The exact structure could not be determined by palpation. The legs were in general similar, but presented some variations. The difference was probably associated with scoliosis and inequality evident in the lower abdomen and pelvis. There was free movement of both limbs at the hips, the only other movable joint being best seen in right leg at the first break below the hip. Some anteroposterior swinging was possible. The feet were misshapen although largely normal. The man's intelligence would be classed as that of a boy of 12. He is able to get around.

Strictly speaking this subject is not a total phocomelus since both femurs are present and well developed, but he most nearly approaches this class because there is no evidence of the presence of any humerus, radius, ulna, tibia or fibula. The cause for the monstrosity is intrinsic, but whatever the force may be it seems imperative that it act, not on the developing embryo, but on the germ plasm of its ancestors.

(1a-28)

**On Sirenomelus.**

*E. Langer, Ztschr. f. Geburtsh. u. Gynäk., 84:131, Stuttgart, Sept. 24, 1921.*

Most authors on this subject have contented themselves with the study of the symposium formation (Foerster), the fusing of the lower limbs, but have ignored the malformation of the inner organs. Classification of syndromes: (1) Sympus apus: Both femurs fused into one thick femur; distally, a bone formation with 2 rudimentary tibias; no foot. (2) Sympus monopus: Thick femur with distal cleft; Rudiments of 2 tibias and of tarsal bones; either few or many toes (5-9); in the latter case the cleft in the femur reaches high up; between the

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double tibial rudiments fibulæ adhered to the bone; several tarsal bones. (3) Sympus dipus; 2 femurs, 2 tibias, 2 fibulas. The foot skeleton complete, only the calcaneum deformed. All parts of the deformed extremities twisted. The patellas lie median in apus; in monopus and dipus more lateral; the great toes lateral, the fibulas median. Anomalies of the other organs are to be found in the bony pelvis and pelvic organs, the urinary apparatus being more deformed than the genitalia. In 21 autopsies the kidneys were deformed in 18. In 7 both were lacking; in 3, only one kidney was found (in 1 case only the microscopic rudiments were present); in 1 case horse-shoe kidney; in the others, cystic kidneys. The ureter was lacking (usually corresponding to the kidney condition). The bladder was lacking in 14 cases. In 1 it was rudimentary. The suprarenal capsules were lacking on both sides, in 6 cases out of 13 and once on one side. Sexual organs: In 1 case quite lacking; in 9 cases testicles and in 7 the female genitalia were present. Anal aperture was lacking in nearly all cases. The intestine ended in a sac filled with meconium in the sigmoid or rectal region. The pelvic bones were always displaced and fused. Absence or rudimentary formation of the lumbar vertebrae and sacrum; often the sacral canal remained open. The musculature of the lower extremities was completely altered. Gluteal muscles were nearly always lacking, musculature of the lower leg completely altered and hardly recognizable in most cases. Nervous system: Absence or rudimentary formation of the plexus sacralis.

Causes of this deformity may be: (1) Mechanical injury: pressure on the uterus, trauma; (2) amniotic disturbances: faulty structure or function of the Wolffian ducts, as these ducts contribute to amnion formation. (3) Endogenous causes, i. e., faulty embryonic rudiment: The author believes it due to an injury of the caudal end of the body involving both the bony-muscular system and the viscera simultaneously though not to the same degree. Although others believe the injury secondary to a predisposition of the segmentary system, Langer thinks the deformation is due to disorders in the beginning of segmentation. The trouble begins at the latest before the end of the third week, i. e., at the period before the urogenital apparatus and extremities take form. It has therefore to do with a very early teratologic formation. External factors as causes are dismissed. As regards the cause of the internal maldevelopment of the embryo nothing is known. Infection or chronic intoxication of the mother (alcohol) has not been proven as a cause. Neither has the occurrence been familial. The fact that in one case a greatly enlarged thymus was found is of no etiologic importance, as the endocrine system is not yet developed at the time when the deformity takes place.

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(1a—29)

**Apparatus for Study of Rhythmic Oscillations Applied to Laboratory Animals.**

*E. Pozerski, Compt. rend. Soc. de biol., 85:702, Paris, Oct. 22, 1921.*

Certain navigation companies requested laboratory study of seasickness. An apparatus has been constructed for observation of oscillatory effects like those to which ship passengers are subjected. Rabbits, guinea-pigs, hens and pigeons have shown no evidence of discomfort even after six hours. Symptoms resembling those of seasickness have been produced, however, in dogs.

(1a—30)

Stereotropic Orientation of the Tube-Feet of Starfish (*Asterias*) and Its Inhibition by Light.

*A. R. Moore, J. Gen. Physiol., 4:163, Nov. 20, 1921.*

To demonstrate the stereotropic orientation of the tube-feet, a starfish was placed on its back in a dish of sea water, and when it had become fairly quiet a foreign body was applied to one of the rays. This caused a retraction of the tube-feet and closure of the ambulacrinal groove, followed by an opening of the groove and a movement of the tube-feet toward the stimulated area. If 2 points on the same side of the ray but at a distance from each other are touched, then the tube-feet turn to that side. The tube-feet midway between the 2 loci of stimulation bend neither toward the one nor toward the other but at right angles to a line joining the 2 points. This constitutes a tropistic reaction analogous to that of heliotropic orientation to 2 sources of light. If the tube-feet as a result of their extension in response to contact touch the surface, they at once adhere by means of their sucking disks. When a considerable number of tube feet have thus taken hold and an attempt is made to pull the animal away from the surface, some of the feet will be torn off and left sticking to the surface. It is possible, however, by means of the light reaction to cause adhering starfish to release their hold. This was demonstrated by placing a starfish ventral side up, in a dish of sea water in a dimly lighted room. As soon as the tube-feet were thrust out a flash of sunlight was thrown across the animal. The tube feet then withdrew and the ambulacrinal grooves closed; the rays bent ventrally. After several seconds in this position the grooves opened and the tube-feet extended. This occurred even with continuous illumination. These experiments with light were further continued in a dark room, the animals being observed by means of red light, while white light was admitted through a shutter for any desired length of time and allowed to illuminate the ventral side of 1 or more rays. It was noted that tube-feet which were not in contact with a surface retracted much more readily in response to illumination than did those which were in contact with a surface, but by the use of more intense light it was found possible to force the retraction of those in contact with a surface. This antagonism between stereotropism and the reaction due to light gives a means of quantitative treatment of stereotropism by the method of indirect measurement. It is therefore only necessary to illuminate the animal with a known quantity of light, just sufficient to neutralize its stereotropism, as shown by the withdrawal of the tube-feet from the surface, in order to have a measure of stereotropism in terms of light quantity. The least quantity of light which will cause the retraction of the tube-feet from a surface may be regarded as the photic equivalent of stereotropism. As the result of experimental measurements the author finds that the average photic equivalent for stereotropism in asterias is between 250 and 350 candle-meter seconds.

(1a—31)

Observations on the Influence of Cerebral Activity on the Secretion of Gastric Juice in Man.

*Heinz Schrottenbach, Ztschr. f. d. ges. Neurol. u. Psychiat., 69:254, Berlin, July 30, 1921.*

After a historical introduction summarizing earlier observations,  
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the author describes experiments carried out under very exact conditions on two patients (a girl of 5 and a man of 59 years) in whom a gastric fistula was made to relieve a total stricture of the esophagus. The method of study included a modification of Nicolai's apparatus for measuring the secretion of saliva. A plethysmograph record of the blood volume of the arm permitted direct inferences of the quantity of blood in the abdominal organs, owing to the antagonism between the blood-vessels of the latter and those of the extremities.

The experiments, illustrated by 6 tables and 32 curves, are classified according to the nature of the stimuli: (1) physiologic (mucous membrane of the mouth), (2) optic associative, (3) acoustic associative, (4) disagreeable emotions, (5) pleasurable emotions, (6) sleep or sleepiness, and (7) attention.

The most important results may be summarized: (1) The secretion is increased by (a) the chewing of food, (b) ideas of food by optic association, (c) ideas of food by acoustic association, (d) the feeling of hunger, and (e) pleasurable emotions (without arousing the appetite). The increase is less after optic associative ideas than after physiologic stimuli (chewing), but the effects of the latter are frequently equalled and even surpassed by acoustic associative ideas. (2) The secretion is decreased by transitory disagreeable emotions. The effect of the stimuli that increase the secretion is counteracted, either lessened or abolished, by (a) permanent latent disagreeable emotions, and (b) sleep. (3) The interaction of these various stimuli causes variations in the increase or decrease of the secretion of gastric juice. The observations concerning the effects of sleepiness, pleasure and displeasure show that the organic utilization of food is greatly affected by fatigue and emotional conditions.

The period of latency between the stimulation and the secretory reaction was ascertained for the first time with exactitude. Hornborg stated that it was 6-7 minutes, and Bickel, 4-5 minutes. The highest figure observed by author was 118 seconds, i. e., under 2 minutes, and that only once in the course of the experiments relating to the physiologic stimulation of the mucous membrane of the mouth, which showed the greatest variation in that respect (from 31 to 118 seconds, with an average of 75 seconds). The average in optic association was 48 seconds and in acoustic association 39 seconds. The reception and conduction of optic and acoustic stimuli is much more rapid than that of gustatory and olfactory stimuli. In other words, this is a partial expression of the specific organization of man with a predominantly optic and acoustic orientation.

A curious similarity was observed between the secretory and the plethysmographic curve in that a sudden strong initial deviation is followed by a gradual return in successive waves or phases. This phenomenon, together with the observation that in 5 of 6 cases the increased secretion was preceded by an increased quantity of blood in the vessels of the digestive organs, points to the probability that the gastric glands are influenced by the vasomotor reaction. There must also be sought a direct nervous influence on the glandular function which regulates the vasomotor activation. A direct nervous influence on the gastric glands is certainly responsible for the variations of the qualitative composition of the secretion.

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**The Intestinal Nervous System.**

*Erik Müller, Upsala Läkaref. Förh., 36: No. 22, Stockholm, Sept. 1, 1921.*

The nerves of the intestinal canal may be divided into two groups: (1) the external and (2) the internal nerves. The first group includes the rami intestinales of the pneumogastric nerve, and the mesenteric and colic nerves of the sympathetic and sacral autonomic nervous system. The second group consists of the plexus of nerves in the walls of the intestine. The author has studied the internal intestinal nerves for the purpose of finding an anatomic basis for the movements of the intestine. He found that the myenteric plexus is differently constructed in the stomach and in the intestines. In the stomach the plexus consists mainly of typical vagus cells. The submucous plexus of *Squalus acanthias* contains mainly sympathetic cells and to a lesser degree, vagus cells. The myenteric plexus of mammals, including man, consists entirely of vagus cells. In the musculature and mucosa of animals interstitial (sympathetic) cells were found. In the small intestine the myenteric plexus consisted in an equal proportion of vagus and sympathetic elements. In the large intestine the sympathetic cells predominated, but vagus cells were also found. The intestinal submucous plexus consists mainly of sympathetic cells.

These observations showed that the nervous structures of the various parts of the gastro-intestinal canal are not uniform, as Cannon and several others have claimed. The author believes that the vagus cells and the sympathicus elements have an antagonistic effect; the vagus cells have a motor and the sympathetic cells an inhibitory effect. From this point of view the intestinal plexus forms a natural basis for the movements of the intestine ("the law of intestine"), as Mall, Bayliss and Starling have proved.

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**Studies of Liver Function. Benzoate Administration and Hippuric Acid Synthesis.**

*G. D. Delprat and G. H. Whipple, J. Biol. Chem., 49:229, Nov., 1921.*

The estimation of functional capacity of the liver cannot as yet be accurately determined. Such a test should include some factor of strain or load which can measure the high and low limits of liver function. They believe the ideal liver functional test would consist in the introduction intravenously of some non-toxic substance which would test by a synthetic demand, the functional reserve of the liver (normal or abnormal), but such a test they do not find at hand.

In the study of this problem the authors recognized the importance of the liver in many synthetic endogenous processes and felt it would be desirable to extend the study of hippuric acid synthesis under experimental conditions. Their procedure was as follows: Dogs which had been fasting three or four days prior to the experiment were used. They were kept in standard metabolism cages and water supplied to them freely. The urine was collected at a fixed hour each day and was subjected to the following analysis: Total urinary nitrogen by the Kjeldahl method; urea and ammonia nitrogen by Marshall's method; free benzoic acid by the method of Raiziss and Dubin; hippuric acid

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by the method of Folin and Flanders; all determinations were made in duplicate with suitable controls. In a few instances sodium benzoate was administered to the animals through a stomach tube, but in the majority of cases the sodium benzoate was injected into the jugular vein of the dog in a 5% aqueous solution at the rate of about 20 c.c. per minute. The authors have tabulated their experimental results to show: (a) the recovery of hippuric acid before and after chloroform anesthesia; (b) the recovery of hippuric acid in the first five hours after benzoate injection intravenously and before and after fifty minutes of chloroform anesthesia; (c) the recovery of hippuric acid in the first five hours after benzoate injection and before and after fatal liver injury due to chloroform anesthesia; (d) the recovery of hippuric acid from the fifth to the twenty-fourth hour after benzoate injection intravenously and before and after chloroform anesthesia; (e) the rise in ammonia, urea, and total urinary nitrogen following benzoate intravenous injection; (f) the effect of gradually increased doses of benzoate on the urinary nitrogen; (g) the rise of urinary nitrogen following benzoate injection prevented by administration of dextrin; (h) the effect of sodium benzoate injections on the blood serum proteins.

In discussing these results the authors point out that the synthesis of hippuric acid in the body following benzoate administration is not prevented by an extensive chloroform liver necrosis, though such an injury will cause a distinct delay in the synthesis and excretion of hippuric acid. They believe this indicates that the liver normally takes part in this synthesis but that other cell protoplasm of the body may be concerned in this conjugation and may in an emergency take over a greater part of the hippuric acid synthesis. This may apply particularly to the intravenous administration of the benzoate. Their experiments showed distinct increases in ammonia, urea, and total urinary nitrogen wherever dosages of benzoate were given intravenously, exceeding a certain amount per pound body weight. Under certain conditions benzoate injection causes a considerable protein breakdown due probably to the acute need for glycocoll which is taken from the body protein molecule. The serum albumin-globulin ratio is not changed by administration of large doses of benzoate.

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**A Technic for Making a Biliary Fistula.**

*F. C. Mann, Lab. & Clin. Med., 7:84, Nov., 1921.*

A new procedure has been devised for making bile-duct fistulas. It has 2 essential features, namely, fixation of the common bile-duct near to the surface before its relation to the duodenum is disturbed, and draining the duct to the exterior. The procedure is carried out in 2 stages. First the duodenum is made fast just under the skin in such a way that the common bile-duct is near to the surface. After healing is complete, the duct is exposed, the distal end tied, and the proximal end left open flush with the skin. The steps of the operation are as follows: Under ether anesthesia a midline or right rectus incision is made and carried as far as possible without opening the pleural cavity. The pylorus and first part of the duodenum are drawn into the wound. A small opening through the mesentery of the duodenum is made about 4 cm. on each side of the point of entrance of the common bile-duct into the duodenum, and between the duodenal wall and the pancreas. All

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precautions must be taken against injuring the pancreas, the blood-vessels between the pancreas and the duodenum, and the major pancreatic duct. Through the openings the peritoneum and afterward the fascia are sutured with No. 2 chromic gut, leaving the duct-bearing part of the duodenum just under the skin. The superficial fascia and the skin are then sutured over the transposed loop of intestine. In closing around and over the ends of the loop too much pressure must be avoided, so as to avoid obstruction. Healing requires from seven to fourteen days. In the second operation a small incision is made over the point of the transposed loop where the common bile-duct is situated. The duct is exposed, tied, and opened so that it will drain at the point where it emerges from the skin. A soft rubber catheter, left in the duct for a day or two, prevents inflammation from obstructing the bile flow. In a few days the fistula is in working order. By passing a catheter into the opening observations can be made on the secretory rate and pressure, and on the movements of the gall-bladder. Animals have remained apparently normal for six months and more. Tendencies to heal are overcome by frequent catheterization.

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**A Technic for the Establishment of a Permanent Pancreatic Fistula with the Secretion of Inactive Proteolytic Ferment.**

*William deP. Inlow, J. Lab. & Clin. Med., 7:86, Nov., 1921.*

The operation may be done in 1 or in 2 stages. The procedure is as follows: Make a curved incision, about 10 cm., through the skin, starting just below the xiphoid process, circling to the right till at its middle the cut is about 2 cm. from the midline. With enough of the underlying subcutaneous tissue to ensure an adequate supply of blood, this skin flap is reflected to the linea alba and the ordinary midline laparotomy incision is made. The duodenum is brought into the wound and turned to the right. The blood-vessels, in the immediate neighborhood of the entrance of the major pancreatic duct into the intestine, are tied and cut. The pancreas is separated from the duodenum at this place and the duct isolated. The transplantation of the duodenum is done by rotating its axis to the right and bringing the 2 edges of the abdominal wall under the duodenum by means of 4 single mattress sutures (No. 2 chromic catgut) which include both fascia and peritoneum, using 2 sutures at each side, with the duct in about the middle of the incision. Openings just wide enough for the duodenum to pass through snugly, without constriction, are left at each end of the wound. In the rotation of the duodenum a small part of the pancreas is brought out of the abdomen and the entrance of the duct into the gut is thereby brought very near the surface. The mattress sutures pass through this part of the pancreas in an oblique direction; the head of the needle should be passed in first and should come out at the juncture of the intestine and the right layer of the mesoduodenum. At each of these points a part of the bowel wall is included in the sutures for secure anchorage. The sutures are tied and the abdominal cavity cut off from the field of operation.

If the time can be spared for a two stage operation, the second step should be made a month later. If earlier, much bleeding takes place from the new formed vessels. The procedure is: The skin at the right

of the initial incision is reflected in its central part for approximately 1 cm., depending on the amount of room needed for the easy reception of the duodenum, which is brought over to the right and fitted into the cavity thus made. Catgut sutures, passing through the peritoneum and muscular coats of the intestine and through the superficial fascia of the abdominal wall, are inserted to maintain the bowel in its new position. The pancreatic duct is dissected free for the short distance which it runs obliquely beneath the serosa of the gut, and is partly severed at the point where it enters the muscular layer. A very fine silk suture, on a small needle, is passed through the free left lip of the duct, a section of a urethral catheter is inserted into the canal for a short distance, and the duct completely severed. The serosa is brought together over the small wound in the intestinal wall by 1 or 2 Lambert sutures. Three other fine silk strands are then passed through the extremity of the severed duct at equal distances. A small stab wound is made in the original semicircular flap of skin just over the point where the duct disappears into the pancreas, and by means of the strands the duct, with the catheter, is brought through the opening. The skin incision is closed by suturing the subcutaneous fascia with catgut and the skin with interrupted linen stitches. The end of the duct is everted and securely fastened to the skin by 4 silk sutures; the catheter is left in place and its free portion allowed to run along the abdominal wall for 4-5 cm. where it is fastened by superficial stitches. The wounds are iodinized and covered with collodion dressings. A metal collar is put on immediately to prevent disturbance of the wound. After three or four days the catheter comes out. For a week or so afterward, a slightly irritating secretion occurs during pancreatic secretion, whether food is given or not. In about a fortnight observations may begin. The slight tendency to closure may be overcome by passing a probe into the opening every second day.

The animals, save for a slight loss after operation, maintain their weight and can be given meat without bad results. To the ordinary milk diet sodium bicarbonate is added to make up the alkali loss. The secretion is completely inactive so far as proteolytic behavior is concerned; it does not injure the abdominal skin. It is activated by enterokinase prepared by Bayliss and Starling's method. The enterokinase solution keeps for months at room temperature. Collection of juice is best made from a metal funnel applied over the duct opening, with the dog tied in a frame. While collection is not being made dogs lick off and thus save the juice.

The important factors are: the intestine is not opened; the point of exit of the duct is fixed directly beneath the skin; the duct is brought to the surface by an incision that is not the operative incision. These things are accomplished by severing the duct just as it enters the tunica muscularis of the intestine, transplanting the duodenum under the skin with rotation of its axis to the right, and making a primary curved incision away from the point of bringing out the duct. The method obviates peritonitis, abdominal stricture, retraction and necrosis of the duct, and subsequent closing of the fistular opening by its inclusion in the operative scar.

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**The Regulation of the Excretion of Water by the Kidneys.**

*J. G. Priestley, J. Physiol., 55:305, London, Nov. 18, 1921.*

The author had previously made observations on the production of diuresis by water drinking and the constancy of the hemoglobin percentage in the blood. In this paper is shown a composite curve giving the average results of 15 experiments, in several of which hemoglobin estimations were made. None of these showed any definite change in relation to the diuresis. It was believed probable that some relation exists between the diuresis and the composition of the blood. As attempts to prepare a semipermeable membrane for measuring the osmotic pressure of the blood before and after drinking were not successful, determinations were made of the water and chlorid content of the blood. In several experiments there was after drinking a slight but distinct increase in the relative amount of water in the blood, as estimated by the loss of weight on drying. Samples (8 c.c.) of venous blood taken by means of a syringe, were examined for chlorid content. The samples were taken (*a*) three hours after a meal; (*b*) eight hours after a meal, during which period no food, drink nor exercise was permitted, and (*c*) a few hours after two liters of distilled water were ingested and during the resulting diuresis. The tabulated results show a diminution of about 5% in blood chlorid after water drinking. This cannot be accounted for entirely by dilution of the blood by the ingested water, for the dilution—as measured by hemoglobin determinations and by the loss of weight on drying—is less than 2.3%. Priestley believes that the absorbed water is taken up in the blood only in limited quantity (about 30 gm.) and that the remainder is stored elsewhere with the salts and probably albumin that have passed out from the blood. To study the excretion of water and chlorids in the urine during water diuresis, observations were made on a subject who ate a breakfast, including a cup of coffee, about 8 a. m., and subsequently received no food or drink until completion of the observations. The excretion of urine fell within several hours after breakfast to about 50 c.c. per hour, remaining fairly constant at about this figure. The excretion of chlorids, however, fell progressively during the day. If after some hours, sodium chlorid, 15 gm. in 75 c.c. of water, was administered, the excretion of urine per hour rose gradually from 70 to 90 c.c. and then slowly fell. In a control experiment in which 100 c.c. of distilled water was given in place of the NaCl solution there was only a slight interruption in the descent of the curve. To determine the effect of pituitrin the ordinary routine was followed with the addition of 1 c.c. pituitrin injected intramuscularly after the ingestion of two liters of water. The pituitrin delayed the onset of diuresis for from four to six hours or more, while the excretion of chlorids and water in the urine fell steadily and the blood chlorids fell from about 0.5 to 0.47% and remained low. Water diuresis then set in and was accompanied by an increased excretion of chlorids.

It is suggested that these results are compatible with regulation of excretion of water by the kidneys of a dual nature: (*a*) a main regulation dependent upon the diffusion pressure of water in the blood, and (*b*) a subsidiary modification of this regulation dependent upon the inability of the kidney to hold back water when the diffusion pressure of the urine is considerably below that of the blood.

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**The Behavior of the Renal Secretory Epithelium with Regard to the Suspension of Finely Granulated Substances Injected into the Circulation.**

*Felice Bernucci, Morgagni, 64:316, Milan, Oct. 31, 1921.*

The author made experiments on rabbits and guinea-pigs, injecting powdered vermillion, red indigo, fine granules of Chinese ink, carmin, and methylene-blue into the jugular vein. He found that the task of accumulating these fine insoluble grains in the protoplasm belongs to the epithelial cells of the convoluted tubules and of the ascending branch of Henle's loop. During this process of appropriation of the grain, which corresponds with a certain functional activity, the epithelial cells were found to be of medium height and somewhat enlarged. Their nucleus preserved a form varying from round to oval. The protoplasm of that part of the cell turned toward the lumen of the tubules, while the grains were within it, was not disposed in the form of small cylinders, but showed zones of density alternating with small areas of rarefaction; it tended rather toward a filamentary form around and under the nucleus. Not all the individual cells of the convoluted tubules took possession of the granules in an equal degree nor in the same period of time, some requiring more than others. The transportation into the protoplasm was done, in all probability, by the plasmatic tubules, which they entered from the blood. Individual varieties of insoluble granules arrange themselves in a healthy kidney during the excretory phase, around the nucleus and toward the lumen of the tubule. The power of surrounding grains of any kind is greatly diminished or lost entirely in cells whose constitution is altered. This happens in any kind of poisoning, and particularly in that from bichlorid of mercury.

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**Unipolar Stimulation and Isochronism of Muscle and Nerve.**

*G. Banu, R. Dériaud and H. Laugier, Compt. rend. Soc. de biol., 85:841, Paris, Nov. 12, 1921.*

In ordinary bipolar stimulation, the reaction time (chronaxia) of muscle and nerve is the same, except in pathologic cases or when chemical substances (curare) are used. The authors found, in unipolar stimulation of frogs, that the chronaxia for nerve is considerably less than that for muscle (one-half to one-third). It is endeavored to explain the phenomenon. The effective, not the instrumental, electrodes must be considered. In unipolar stimulation, with the negative electrode on the nerve, the current from this cathode approaches the nerve from a diffuse anode, or virtual electrode, situated in the tissues about the region of contact between the nerve and these tissues. Thus the anodal region may be very near the differential cathode. It is known that, if the electrodes are very near each other, chronaxia may be considerably diminished, because of the reciprocal cathodal and anodal polarization. Experiment should show that, with the position of the cathode unchanged, and the anode moved about, the chronaxia of the nerve would be less when an effective anode was created nearer the differential cathode. The results coincided with this hypothesis.

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**The Evolution of Nerve Muscle Mechanisms.**

*S. Bent Russell, J. Comp. Psychol., 1:395, Oct., 1921.*

In tracing the development of nerve muscle mechanisms, one must bear in mind the evolution of other organs and the evolution of the individual as a whole. It is known, for example, that at one stage of evolution, the highest form of animal was like a caterpillar, made up of a chain of similar segments. Each segment had an individuality of its own. The nerve muscle mechanisms of each segment was under separate control to some extent. Each segment had its own segmental head centers. Signal lines connected the segmental head centers. This accounts for the nervous architecture of vertebrates with its spinal system of nerve centers. The primitive organism reacted to changes in its environment, the responses being in the form of molecular changes not limited to definite regions. It came about that the intermittent release of energy in molecular changes in certain regions, produced movement. Periodic energy-releasing cycles causing movement were established. It only became necessary to develop structures which would confine energy-releasing changes to more prescribed regions. In this manner, motor organs, paths of communication and sense organs were developed. Further differentiations and development produced structures that served to condition responses so that behavior was determined by individual experience. Along with the differentiation of sense organs there came also a differentiation of regions having a special sensitivity, giving mechanisms that registered in correspondence with the environment. It is by means of these mechanisms that man is aware of his environment.

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**The Nature of the Isometric Twitch.**

*W. Hartree and A. V. Hill, J. Physiol., 55:389, London, Nov. 18, 1921.*

Experiments were made upon a variety of questions arising in connection with the isometric muscle twitch. (1) The building up of the prolonged contraction results from the summation of the responses to a long succession of individual shocks. Tensions are additive, and if the isometric response to any later shock were the same as or similar to the response to the first shock, the resulting contraction could be obtained simply by summing a series of shock curves of appropriate size, placed at regular intervals along the time axis. But the authors found that no succession of similar responses, corresponding to shocks up to but not beyond the end of the tetanus, is capable of being summed to give the observed curve of prolonged contraction, but that it is necessary to assume that the response to a later stimulus is different from and more drawn out than that to an earlier one. This conclusion was tested experimentally. (2) The temperature coefficients of various characteristics of the isometric twitch of the frog's sartorius muscle were analyzed experimentally. The muscle was stimulated directly by a maximal induction shock, recording its mechanical response photographically (illustrated) on a rapidly moving drum by means of a tension device of short period and high sensitivity. The initial extension of the muscle was comparatively small. It is clear that a more vigorous response at the same temperature will show a

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greater maximum rate of rise of tension, and it is necessary, in order to allow for alterations in the mere size of the response, to divide the maximum rate of rise of tension by the maximum tension. In this way is obtained the "maximum rate of proportion rise" of tension, a quantity of dimensions minus one in time and similar to the velocity constant of a chemical reaction. It is this quantity whose temperature coefficient was determined. The temperature coefficient of the rate of development of the mechanical response is practically constant for different muscles. The average for all experiments was 2.56 for 10° C. (3) The recovery process of the contractile change was considered. If two maximal shocks be sent into a muscle in succession, at any desired interval, the thermal or the mechanical response of the muscle to the second shock can be determined. It was found that under all conditions there is a phase of supernormal heat-production. This phase represents the true "staircase effect" in skeletal muscle. Its duration is much longer than the phase of supernormal excitability in nerve but much shorter than the phase of supernormal contractility in cardiac muscle. Curare increased and maintained the contractile power of a muscle placed on a thermophile insulated with shellac.

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**The Electric Response of Denervated Muscle.**

*E. D. Adrian and D. R. Owen, J. Physiol., 55:326, London, Nov. 18, 1921.*

To determine whether any change in the electric response of a muscle occurs when the nerve-endings have degenerated, a number of frogs were anesthetized with ether and the sciatic nerve was cut high up in the thigh so as to sever its path to the sartorius and the gastrocnemius. At different times after the operation the frogs were pithed, one or both muscles of either side were removed and their electric changes compared. Most of the observations were made on the sartorius which was stimulated at the pelvic end before and after destroying the tibial end with a hot wire. The electric response was led off by electrodes on the tibial end 16-20 mm. away, and was photographically recorded. After each experiment the muscle was treated with methylene-blue. Nineteen days after the operation the nerve-endings had disappeared from most of the muscle fibers on the denervated side and were represented by only a row of fine dots in the remainder. After thirty-six days no traces of nerve-endings were found. None of the denervated muscles failed to give an electric response. The rate of conduction was slightly faster in the denervated muscle than in the control, but in other respects there was very little difference. Previous workers had observed that a stimulus to the gastrocnemius may give a contraction without any electric response; the authors found such to be the case only when the stimulus was weak and the leading-off electrodes were shifted as far as possible from the stimulating electrodes. In such a case the stimulus affects fibers at only one end of the muscle and the tissue between the two leading-off electrodes remains inactive. When the leading-off electrodes were arranged to include the active fibers an electric response was always detected.

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**The Functional and Developmental Relations of the Nervous Mechanism.**

*Donald A. Laird, Med. Rec., 100:890, Nov. 19, 1921.*

In vertebrate development the nervous system occupies an intimate and fundamental relationship to the organism as a whole. Through stereotyped thinking it is easy to assign to the nervous system a priority in development which more pertinent facts do not warrant. The developmental relations of the nervous system should be considered from a functional point of view, for functionally, the unit is a neuromuscular mechanism. Irritability, conductivity and contractility are common property of all protoplasm. In nerve-cells irritability and conductivity are emphasized by specialization, whereas in muscle cells contractility is emphasized. Unicellular organisms, in which the protoplasmic properties are unspecialized, can react and successfully adapt themselves to their environment without the aid of nervous structures. The most primitive multicellular animals have no nervous structures, but some of the cells have the property of contractility developed in advance of the others and these contractile, primitive muscle cells are the first part of the neuromuscular mechanism to develop. The next part of this functional system to develop is the rudimentary sense cells which are morphologically nervous in character as well as in function. Later the so-called motor neurons and the associational or intermediary neurons have developed. The developmental relations of these latest parts of the functional mechanism are not traced in this paper, but they consist in a centralization of structure and organization of relationship of increasing complexity with increase of complexity of behavior and position in the animal scale. Embryologic development of the higher vertebrates and man repeats in a modified way the essential steps of this relationship. In the adult man structures are also found which functionally demonstrate the stages in the developmental origin of the nervous system. These stages of development in the order of their occurrence are: effectors, receptors, intermediaries.

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**The Cerebrospinal Fluid in Relation to the Bony Encasement of the Central Nervous System as a Rigid Container.**

*Lewis H. Weed and Walter Hughson, Am. J. Physiol., 58:85, Nov. 1, 1921.*

The authors made two series of observations on animals (cats). In one series the bony calvarium on one side was largely removed without opening the dura; in the other series a smaller bony opening was subsequently sealed, restoring the intact cranium. In both types of experiment, therefore, the central nervous system remained rigidly protected against expansion outward by the unopened inelastic dura; collapse of the dura in the first series could easily occur, while in the second type of experiment, opening of the cranial cavity could at any time be effected by removing the sealing mechanism. Under these conditions, injections would, the authors believed, give information, by their effect upon the pressure of the cerebrospinal fluid, regarding the relation of the cranial vault to the rigid character of the bony coverings of the central nervous system.

Following the procedure described in the preceding paper, the carotid arterial pressure, brachial venous pressure, cerebrospinal fluid pressure and urinary output were determined in the etherized cats of both series..

The tabulated results of the authors show that repeated intravenous injections of strongly hypertonic solutions fail to reduce the pressure of the cerebrospinal fluid to negative values in animals in which the bony skull over one cerebral hemisphere has been removed. But negative pressures of the cerebrospinal fluid are obtained by intravenous injections of strongly hypertonic solutions in animals in which the opening through the skull has been subsequently sealed; under these experimental conditions, opening of the cranium by removal of the sealing device causes an immediate rise in the pressure of the cerebrospinal fluid to positive readings.

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**Experimental Studies on Hydrocephalus.**

*J. C. Nanagas, Bull. Johns Hopkins Hosp., 32:381, Dec., 1921.*

Young animals were rendered hydrocephalic by Weed's method of introducing a suspension of lampblack into the lateral ventricles or into the subarachnoid space. The escape of cerebrospinal fluid into the subarachnoid space and its absorption there are thus prevented by the sterile inflammatory process set up by the lampblack, and the fluid backs up in the ventricles. The pressure of the fluid in the ventricles becomes much higher than in normal controls, but it can be altered by varying the osmotic pressure of the blood-stream by hypotonic and hypertonic salt solutions. This and direct histologic evidence gained by the Prussian blue reaction after the introduction of iron ammonium citrate and potassium ferrocyanide into the ventricles prove that there is both in the normal and the hydrocephalic animals a pathway for absorption of cerebrospinal fluid through the ventricular ependyma into underlying capillaries. With this absorption the choroid plexuses have nothing to do.

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**Vegetative Reflexes.**

*P. Hartenberg, Presse méd., 29:919, Paris, Nov. 19, 1921.*

The reflexes of the sympathetic nervous system are divided into 2 main classes, the dynamic and the humoral. Dynamic reflexes are classified as follows: (a) Intravegetative reflexes, by means of which several parts of the vegetative system are united. Examples are found in the numerous reflexes which, starting from an irritation in the respiratory tract, heart or digestive organs, are carried over by the vagus to the sympathetic nervous system. In hepatic, nephritic, intestinal or uterine colics various reflex disturbances of the peripheral circulation are produced through irritation of the splanchnic nerves. (b) The sensory vegetative reflexes, include those which are started by a sensory stimulation. Percussion of the seventh cervical vertebra produces a stimulation of the entire vagus and an increase in the tonus of the organs it supplies, while pressure between the third and fourth dorsal vertebrae is supposed to inhibit the vagus. The response of the sympathetic nervous system to thermal sensations is quite definite and extensive and it may appear both locally and also at a distance. There is a sort of

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a compensatory action between the vascular supply of different parts of the body. Vasoconstriction of the skin, for instance is accompanied by a vasodilatation of the viscera, and a similar relation exists between the head and the extremities. Certain affections which arise from exposure to cold seem to be due in part to the intense congestion of internal organs produced in this manner, which favors the growth of pathogenic organisms. (c) The psychic vegetative reflexes are produced by emotions and sensations, which induce cardiovascular, enteric, and secretory instability. (d) Sensory and motor vegetative reflexes, starting from a visceral stimulation, are responsible for a large variety of peripheral pains. All these have the following characteristics: the pain is usually median even when the diseased organ is situated laterally. The pain is not decreased by moderate chloroform narcosis and is never exactly defined. It is felt rather in the muscles than in the skin. Artificial stimulation with hot applications prevents the passage of painful irradiation to the hyperalgesic zone. The pain is increased by intense emotions. Irritation of the viscera also produces muscular reactions, such as contracture of the abdominal wall in peritonitis, and sometimes general convulsions.

Humoral reflexes include: (a) neuro-glandular reflexes. In this case stimulation of the sympathetic nerve produces a secretion of the endocrine gland which is connected with it. (b) Interglandular reflexes, produced by the secretion of one gland on another, independently of the nervous system. The hormone of the corpus luteum, for instance, excites the mammary gland, while others, such as the thyroid and pancreas, inhibit each other. (c) Neuro-glandular reflexes, where the products of internal secretion either stimulate or inhibit the vagus or sympathetic nerve. Examples are furnished by the pancreatic secretion which stimulates the vagus, while adrenalin excites the sympathetic nerve, which in turn produces an inhibition of the functions of the stomach.

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**Action of Hypertonic Ringer's Solutions on the Isolated Heart of *Helix Pomatia*.**

*H. Cardot, Compt. rend. Soc. de biol., 85:813, Paris, Nov. 5; 1921.*

Hypertonic Ringer's solutions cause a brief period of irregular action in isolated snail heart, followed by establishment of slow and regular rhythm, the systoles being generally fuller than those produced by hemolymph or physiologic salt solution; the duration of systole is increased, but less, proportionally, than that of diastole; tonus is diminished. The brief, irregular period is followed by 2 types of action, which are shown in graphs. The effect may be modified by placing the ventricle in a physiologic Ringer's solution before immersing it in the hypertonic Ringer. Contractions produced by the hypertonic Ringer are augmented by change to the physiologic solution. The reactions described are the same whether the ventricle is isolated or completely or partially attached to the auricle.

(1a—47)

**On the Path of Conduction Between Auricle and Ventricle in the Amphibian and Reptilian Heart.**

*D. T. Barry, J. Physiol., 55:423, London, Nov. 18, 1921.*

The atrioventricular ring was tied with silk in four chief segments  
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or quarters, a ventral, a dorsal, and two lateral, although some ligated portions included parts of two segments. It was found that in the amphibian and reptilian heart the atrioventricular funnel does not conduct as a whole. Every segment, with the possible exception of the dorsal, is capable of conducting. There is least resistance to auricular impulses in one comparatively small segment which is placed ventrally and to the left. Reverse conduction has no smooth path open for it; a certain degree of resistance seemed to be more or less uniform in all those segments which are capable of downward conduction, and therefore the upward and downward paths are not necessarily one and the same when the two rhythms alternate. Automatic properties were exhibited more markedly by the dorsal portion and sides of the ventricle base than elsewhere, which indicates, it is believed, that these are not correlated with the chief conducting function.

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**On the Relation of Pulse Pressure to the Output of the Heart.**

*Ruth Skelton, J. Physiol., 55:319, London, Nov. 18, 1921.*

It has been suggested that the pulse pressure might be taken as a measure of cardiac output, and that the pulse pressure multiplied by the pulse rate and then by some constant factor which possibly varied with the individual, might be equal to the minute-volume of the heart. The subject was investigated experimentally by heart-lung preparations on dogs. Hirudin was not used, but the preparation was kept active with defibrinated blood alone. In the first experiment the pulse pressure was determined by recording the oscillations of the arterial pressure close to the aorta with a Frank manometer connected by a rigid tube with the arterial system. The pericardium was retained intact throughout. In the second experiment the arterial pressure was measured by a Hurthle spring manometer. Observations were made with the pericardium closed and open. In each case the manometers were calibrated against a mercurial manometer at the end of the experiment. From the tabulated results it is concluded that the product of pulse pressure by pulse rate is of no value as a measure of heart output. The relation between these two quantities varied between 6.5:1 and 47:1.

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(1a—49)

**A New Sphygmographic Spring Oscillographic Apparatus.**

*Frank L. Soler, Presse méd., 29:930, Paris, Nov. 23, 1921.*

This apparatus was devised to make possible the permanent recording of the oscillations produced by Pachon's oscilloscope, by means of tracings on a revolving cylinder. The apparatus consists of a pneumatic chamber divided into 2 portions by a movable diaphragm. One of these is connected with the tracing device, the other with a manometer and the pneumatic band which is placed around the arm of the patient as in blood-pressure instruments. An increase of pressure in that portion of the apparatus drives the movable diaphragm to some extent into the first portion of the pneumatic chamber and so moves the recording needle. The main feature of the instrument is a spring inserted in the first portion of the pneumatic chamber and fixed on the diaphragm, which forces it back to its previous position after the pressure is withdrawn so that the movements of the diaphragm follow all changes in pressure produced by pulsations.

With this instrument sphygmographic and oscillographic records are obtained under known pressure conditions. Used as a sphygmograph together with a cardiograph, it enables the operator to detect delays in the pulse wave. With a double oscillograph connected with the 2 arms and a cardiograph, delays in the pulse wave in one arm may be determined with precision in cases of aneurysm. Figures identical to those obtained with Pachon's apparatus are obtained for the maximum and minimum blood pressure.

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**Mechanism of the Heart Action during Pressure on the Eye-ball.**

*E. Jenny, Ztschr. f. d. ges. exper. Med., 25:89, Berlin, Oct. 14, 1921.*

The author showed in a previous investigation that Aschner's reflex is physiologic in children; among 250 children it was absent in only 4.4%. He has now obtained graphic representations in 120 cases, and 85 electrocardiograms of the heart action. In 120 children and young adults, the heart action, during pressure on the eyeball, or on the supra-orbital nerve was graphically registered, the catgut galvanometer being used in 85 cases. In every instance a chronotropic vagus action was noted, causing inhibition of the heart-beat for as much as eight seconds. In addition to auricular, and in one case ventricular, extrasystoles, automatic beats, single or in series, were frequently recorded. They originated in the coronary process, in the main portion of the Tawara node, in the crus commune of the bundle of His and in the path of stimulation below the division. Twenty-three times the P-curve became smaller or disappeared entirely, which may be explained by the changed position and blood content of the heart during pressure on the eyeball.

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(1a—51)

**The Venous Supply of the Heart.**

*R. Burton-Opitz, Am. J. Physiol., 58:226, Dec. 1, 1921.*

In his study of this subject, the author first determined experimentally the influence of occluding parts of the pulmonary circuit. Etherized cats were used and an opening made in the chest wall by resecting the ventral portion of several ribs. Artificial respiration was instituted and a screw clamp applied to the hilum of either lung and allowed to remain in position throughout the experiment. In a number of additional animals, the pulmonary artery was carefully isolated from the neighboring tissues to permit the application of clamps of similar construction to various branches. The carotid artery was then connected with a mercury manometer. The venous inflow into the heart was registered by means of a recording stromuhr inserted into the inferior vena cava. The record of each experiment embraced the tracing of the carotid blood pressure in relation to the curve of the pressure prevailing in the inferior vena cava. In addition it showed the calibration of the venous blood stream, as well as the abscissa for the pressures and the second-marks of a Jacquet chronograph. The procedure then consisted of temporary compression of the left superior branch, left middle branch, and entire left or right pulmonary artery. The experimental conditions were kept uniform throughout these tests.

The pulmonary ventilation was adjusted at a constant level, yielding a moderate expansion of the lungs. The procedure followed in each case consisted in obtaining a sufficiently large number of stromuhr-phases from which the normal flow and pressures could be calculated. Then followed the compression, lasting anywhere from one to five minutes, and accomplished by closing the clamp which had been previously applied to the vessel. The tabulated results show that the blocking of even a single superior branch induces a fall in carotid pressure and an increase in the venous pressure as measured in the inferior vena cava near the right auricle.

To determine the effect of varying degrees of ventilation of the lungs, the author performed experiments during rhythmic artificial respiration with the right side of the chest widely opened. The right bronchus was then isolated and so placed that it could be compressed at any time by means of a clamp. A small perforation was made in this bronchus distally to the clamp and the opening closed immediately with an artery clip. The author was thus enabled to impart to this lung any desired degree of collapse while the other lung received rhythmic currents of air. The results showed that the venous supply of the heart and, therefore, its output as well, were markedly affected by the activity of the lung. The most efficient flow was obtained when this organ was retained in a state of distention equalling that of its normal expansion. Increasing degrees of ventilation led to a reduction in the venous supply of the heart, a rise in the venous pressure, and a fall in the carotid pressure. The decrease in the venous supply of the heart is referable, the author says, to a mechanical hindrance to the blood flow through the lungs.

To determine the effect of partial and total compression of the pulmonary artery, the author used a special clamp so that the desired amount of compression of this vessel could be obtained. Such a procedure he found, led to a reduction in the venous return, an increase in the venous pressure and a fall in the carotid pressure. In determining the effects of tricuspid regurgitation, he employed a specially devised cannula which when inserted between the valve flaps gave rise to a degree of regurgitation which produced a decisive rise in the venous pressure and very significant decrease in the caval blood flow. In all these tests the carotid blood pressure suffered a marked decrease. The condition of aortic stenosis was simulated by constriction of the aortic orifice. The results were a rise in the caval pressure, reduction in the venous supply of the heart and a marked fall in the carotid pressure. In his study of the changes evoked in the circulation of the inferior vena cava in consequence of occlusion of the arteries of the head, the author found that the blood flow in the inferior cava is decidedly increased by the compression, and that equally conspicuous rises take place in the arterial and venous pressures.

To determine the effects of compression of the thoracic aorta upon the blood flow in the inferior vena cava, Burton-Optiz compressed the aorta at a distance of about 5 cm. above the diaphragm. Immediately after occlusion of this vessel, the flow in the inferior cava decreased from 5.38 c.c. in a second to 0.09 c.c. in a second, while the caval pressure decreased from 1.6 mm. Hg to 0.8 mm. Hg. These values were retained throughout the period of aortic constriction. The carotid pressure, however, increased from 92.6 mm. Hg. to 108.8

mm. Hg. Following occlusion of the thoracic aorta, the circulation through the vessels of the head and forelegs may be decidedly increased and an increase in pressure in the superior vena cava was also observed.

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**The Pulmonary Circulation Time, the Quantity of Blood in the Lungs and the Output of the Heart.**

*G. N. Stewart, Am. J. Physiol., 58:20, Nov. 1, 1921.*

If  $V$  is the minute volume of the heart,  $Q$  the volume of blood in the lungs and  $T$  the mean pulmonary circulation time (in seconds), then

$$V = Q \frac{60}{T}$$

The 3 quantities have not all been measured in any one animal, but each has been measured by different observers both in animals and man. The object of this paper is to publish observations made on dogs twenty-five years ago. The question of a possible relationship between  $T$  and the surface area of the animals experimented upon is discussed in detail with numerous mathematical formulas. Regarding the time of the lesser circulation (in dogs)  $T$  is practically always obtained in the form of a crude number (time from a vein, usually the external jugular, to a systemic artery, usually the carotid). A correction must therefore be applied for the time from the left ventricle to the artery. This correction is as small as possible, in determinations made without opening the chest, when the point at which the arrival of the salt or pigment is noted is on the carotid low in the neck. In the author's experiments salt or methylene-blue solution was injected from a syringe through a cannula in the jugular vein low in the neck or through a catheter passing into the superior vena cava. The lost time is practically negligible since the solution reaches the heart almost as soon as the injection begins. One may therefore disregard the lost time between the point of injection and the heart. A distant vein such as the saphenous should not be used for injection, as the necessary correction cannot be accurately measured by calculating from the average velocities in the veins as given in text books. Another correction concerns the time lost in the heart according to the point in the cardiac cycle at which the first of the solution enters the right ventricle. When the heart is beating rapidly this factor is negligible.

For the direct estimation of the quantity of blood in the lungs, the pulmonary artery (or right heart) was blocked alone, or the aorta (or left ventricle) alone, by the sudden injection of melted paraffin through a catheter passed into the jugular vein or carotid artery. The precise distribution of the paraffin was determined post-mortem. The lungs were ligated and generally the heart also, and the blood in them estimated colorimetrically. The author found that when the outflow through the aorta was completely blocked, the inflow into the right heart being unobstructed, or at least the inferior cava open, the lungs contained 22% of the total blood in one animal, and the heart and lungs together 27% and 30%, in 2 animals. When the block on the right side was complete, or at least when the pul-

pulmonary artery was entirely blocked, while the outflow from the left side of the heart was either entirely free or only partially obstructed, the lungs contained 6, 9, 7, 3.5 and 5% of the total blood, in 5 animals. When both sides of the heart were completely obstructed simultaneously, the lungs contained 21% and 18.6% in 2 animals. In an animal bled to death the lungs contained 3% of the total blood. In an animal killed by passing a strong current through the heart the lungs contained 9%, and the lungs and heart together 25% of the total blood.

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**An Investigation into the Circulation through the Lungs.**

*S. W. F. Underhill, Brit. M. J., London, Nov. 12, 1921, p. 779.*

The adaptability of the pulmonary circulation was tested by imitating in animals, as far as possible, the condition of embolism of one main branch of the pulmonary artery as it occurs in man. Experiments on cats under ether are described; the following conclusions drawn: (1) Ligature of left pulmonary artery in cats (chest open, under artificial ventilation) causes rise of pulmonary blood-pressure of about 40%. No effect observed on carotid blood-pressure, pulse rate, output of heart, or state of dilatation. (2) The healthy heart can accommodate itself to sending same volume of blood through one lung only, in a given time, as it previously sent through both. (3) No mechanism producing slowing of heart from rise of pulmonary blood-pressure was demonstrated. (4) If chest is closed after artery has been ligatured, the animal remains in good condition; frequently the condition is improved. Respiratory rate is faster than normal (frequently about double) but the depth tends to be shallow. (5) Saturation of the blood after ligature is about 75%; if artificial ventilation is increased (within normal limits) complete saturation can be obtained. This is not the case with animals in which the chest has been closed and artificial ventilation discontinued; in these, saturation remains at about 70%. (6) Examination of lungs shows increased quantity of blood in right lung, due to twice the normal volume flowing through it in a given time. Left lung, after ligature of left pulmonary artery, under artificial ventilation, contains almost no blood, except a little in veins. After the chest is closed and animal allowed to breathe naturally, it contains more blood than the right lung, exhibiting a varying degree of congestion. This blood comes from the bronchial arteries and stagnates in the pulmonary capillaries. (7) Ligature of the right bronchus causes small immediate rise in pulmonary blood-pressure without affecting carotid pressure. (8) Saturation of the blood has always been under 90% even when artificial ventilation has been increased. (9) There is presumably still a certain amount of circulation through the right lung under these conditions. Further investigations are proceeding.

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**Researches on the Circulation Time and on the Influences Which Affect It. V. The Circulation Time of the Spleen, Kidney, Intestine, Heart (Coronary Circulation) and Retina, with Some Further Observations on the Time of the Lesser Circulation.**

*G. N. Stewart, Am. J. Physiol., 58:278, Dec. 1, 1921.*

The author describes in detail his experiments on dogs, cats and  
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rabbits as to the circulation time; in the test of the pulmonary circulation time, one bullfrog was used. The electrical method (with galvanometer or telephone) and the pigment injection method (with methylene-blue) were employed and identical results obtained. The circulation time of the spleen was measured in a number of cats and dogs. When the organ was protected from exposure and cooling, the time was not more than the pulmonary circulation time—about four or five seconds; but when the organ was exposed and cooled, the circulation time increased to as much as eleven seconds. Stewart suggests that these changes to which the circulation times of the kidney and intestines are equally susceptible, are due to local vasoconstriction aided, possibly, under conditions of shock by the stagnation of blood in the capillaries. In rabbits the circulation time of the kidney was found to be about six to eight seconds, which could be lengthened by exposure and cooling. Such factors were found to have the same effect on the circulation time of the intestines (normally about three seconds), and of the testis (normally less than four seconds). The coronary circulation time was estimated in rabbits and dogs to be about two to three seconds. No obvious effect was observed by the author during stimulation of the vagus, unless the heart was stopped completely. The circulation time of the retina was estimated by injecting a solution of methylene blue in physiologic saline into the cardiac end of the external vein in rabbits, and observing with the ophthalmoscope (indirect method) the arrival of the pigment at the central artery and vein. This circulation time was found to be one of the shortest, if not the shortest, measured in these experiments, being less than two seconds in some of the rabbits.

The author performed one experiment on the pulmonary circulation time on a curarized bullfrog in which the cerebral hemispheres had been destroyed. Methylene blue (0.2% in 0.5% sodium chlorid solution) was injected through a hypodermic needle into the ventricle. The arrival of pigment in the lung was observed under the microscope by reflected light. The circulation time to a middle-sized branch of the pulmonary artery was three and two-tenth seconds; to a similar pulmonary vein tributary ten and two-tenths and twelve (average ten and eight-tenth) seconds. The net pulmonary circulation time was seven and six-tenth seconds.

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**Studies on the Physiology of Capillaries. II. The Reactions to Local Stimuli of the Blood-Vessels in the Skin and Web of the Frog.**

*August Krogh, J. Physiol., 55:412, London, Nov. 18, 1921.*

In these experiments medium or small specimens of *Rana temporaria* were used, generally narcotized with urethane, though most of the observations were made on curarized or normal frogs. The web was spread on glass plates, and magnifications between 40 and 60 diameters were employed. The capillaries in the skin and web are contractile and react independently of the arterial pressure. This fact was determined by mechanical stimulation of the capillaries with stimuli of varying intensity. The direct application of 0.001 cm. of 0.1% adrenalin on the skin or web just over the superficial branches (Sec. 1—Page 36)

of arteries, affects only the larger arteries, viz., those about 0.1 mm. and upwards in diameter. Adrenalin causes contraction of all the arteries in frog's muscles, but not of the capillaries.

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**Spontaneous Rhythm of the Arteries and the Exchange of Fluid Between the Blood-Vessels and Tissues.**

*Hermann Full, Ztschr. f. klin. Med., 91:290, No. 3-6, Berlin, 1921.*

The rhythmical twitching of excised sections of arteries was studied in previous experiments. For the present investigation, rings of blood-vessels, 1.5 cm. in width, were first stretched by a weight of 100 gm. for three-fourths of an hour in a vessel containing 150 c.c. of Locke's solution. Three or four drops of a 1% solution of adrenalin were then added to the solution and the weight was reduced to 20 gm. The lower end of the vascular ring was attached to a glass rod and the upper end was fixed to a recording lever. Oxygen was passed through the fluid to exclude the possible effects of asphyxia. The arteries of horses react at once to adrenalin by rapid twitching and relaxation, while the arteries of cows show rapid twitching but slow relaxation. Rhythmic twitchings set in after one or even two hours. In contrast to the earlier results, the first contractions were not the strongest, but they gradually increased later and then decreased. The addition of quinidin (10 drops of a 1% solution) decreased the rhythm, and the musculature as well as the nerve-endings were apparently paralyzed. The tonus of the vessel remains unchanged by quinidin, but atropin stops the rhythmic contraction.

Solutions of dextrose stimulated the rhythm only after the twitchings had already begun, while the addition of water increased the rhythm to a lesser degree.

The arteries will show rhythm even after several days if they are kept on ice in Locke's solution. Adrenalin causes not only contractions but also alternating vascular dilatations. Scholz (1911) has shown that adrenalin, injected intravenously into animals with kidney disease, produces an increase of pressure, and that there is a second rise even higher than the first, during the fall of the initial rise. His explanation was that adrenalin caused local vessel spasm at the point of injection, thus disturbing the further absorption of the drug, while the adrenalin was diluted by the body fluids to a point at which it was below the concentration necessary to produce an effect. This explanation is incorrect because adrenalin causes a concentration of the blood. The observation that a fall in blood-pressure follows the initial rise is explained by the fact that there is a peripheral vasodilatation along with the vasoconstriction; the latter is much more powerful than the former was at the beginning, but the dilatation lasts longer than the vasoconstriction. If the contractions which were observed in the excised pieces resemble those occurring in the body, there must also be variations in the blood-pressure.

The different waves of variation in the blood-pressure, caused by either peripheral or central conditions, correspond to the contractions of the excised portions, especially those variations in the blood-pressure which are rhythmic and which were described by Biedl as following the subcutaneous injection of adrenalin. The author studied the effect of adrenalin on human beings by using the results of the

blood-pressure determinations with a Riva-Rocci apparatus. Pressure was measured every two or five minutes. This repetition causes a possibility of error, in that the repeated interruption and freeing of the circulation may cause variations in the pressure. Accordingly, only very marked variations are useful in determining the result.

It occurred to another investigator (Gaisböck) that there is a striking improvement in nephritis after the adrenalin has caused a transient increase in pressure, with a feeling of oppression. This improvement is only subjective. The author reports a case of glomerulonephritis in which a striking turn for the better occurred after the intramuscular injection of 0.25 mg. of adrenalin. The pressure rose at first, then fell and rose again, with a marked fall at the end. The author does not class these variations with the rhythmic contractions of the vessel-wall. Rhythmic variations are not as yet demonstrated in human beings, at least, not beyond doubt. The significance of the observations in man consists in the fact that there is a concentration of the blood after a rise in blood-pressure, which is followed by an out-pouring of fluid from the blood into the tissues. The reverse, that is, dilution of the blood, occurs when the pressure decreases.

The author's experiments on rabbits showed that even moderate variations in the pressure (a rise of 40 mm.) caused a distinct increase in the number of erythrocytes of from 300,000 to 600,000. Increase of pressure after adrenalin (1 mg. subcutaneously) with a rise of from 60 to 70 mm. caused an increase of the red-cells of 1,250,000. The author observed an increase of the erythrocytes to nearly double the original number after the injection of adrenalin in 3 cases (of leukemia, hemolytic icterus and late rickets). In another case of arteriosclerosis with retention of urine, caused by an hypertrophied prostate, the author observed a fall in pressure after the bladder was emptied and, every time the blood-pressure fell, there was a coincident drop in the number of red blood-corpuscles.

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**Studies on the Visceral Sensory Nervous System. IX. The Readjustment of the Peripheral Lung Motor Mechanism after Bilateral Vagotomy in the Frog.**

*T. L. Patterson, Am. J. Physiol., 58:169, Nov. 1, 1921.*

Previous workers (Carlson and Luckhardt) have observed a condition of hypertonus in the lung of the frog after vagal section. The object of these experiments was to determine whether such hypertonic condition is permanent or temporary.

The observations were made on the common frog (*Rana pipiens*). Healthy animals were selected in pairs, one of which was kept as a control, while in the other, one or both vagi were sectioned in the region of the neck, after anesthesia. After recovery, direct observations were made on the visible changes in the contour of the flanks, and on the external respiratory movements of the animal, and were compared with those of the control. During the period of observation the paired animals were kept in small compartments in a large vivarium provided with running water, and were fed caterpillars and earthworms. To further control any possibility of depression in these animals resulting from the confinement, the vagi were sectioned in many of the control animals 5 to 8 weeks after the cutting

of the nerves in the first animal, but the reaction was usually the same in both cases.

Bilateral vagotomy in the frog destroys the inhibitory control over the peripheral lung automatism, leaving it free to exert its full influence on the lungs so that the lungs contract and become hypertonic to the point of nullifying their function. The normal contour of the flanks disappears and the body-line becomes straight or even curved in. In unilateral section of the vago-sympathetic nerve there is loss of the inhibitory control over the peripheral lung automatism, on the side of the section only. In both unilateral and bilateral section of the vago-sympathetic nerves there is a gradual physiologic readjustment of the peripheral lung motor mechanism which usually starts from twelve to twenty-one days after the nerve section, when the lung begins to be distended by swallowed air, pushing out the flank and finally forming olive shaped prominences. This readjustment was partial in all the animals except 1, which lived for a little over eight months, the complete physiological readjustment occurring at the end of about seven and one-half months. In other animals living for a period of from two to five months, those of five months' standing always showed more physiologic readjustment than those of less duration. In animals recently bilaterally vagotomized, up to periods of from two to three weeks, air is found more constantly and in greater amounts in the stomach and intestine than in similarly treated animals of longer standing. This indicates that air is forced into the stomach by the act of swallowing, because of the persistently constricted lungs. Autopsy findings confirmed the results observed.

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**The Relation of Respiration to Rhythm in the Cardiac Ganglion of Limulus Polyphemus.**

*Walter E. Garrey, J. Gen. Physiol., 4:149, Nov. 20, 1921.*

In his study of the CO<sub>2</sub> production by the cardiac ganglion of *Limulus polyphemus*, Garry has shown in previous communications the definite relation between the rate at which the neurogenic heart beats and the intensity of the respiration of the nerve-cells which develop the rhythm. In this paper the author discusses the agencies which stimulate the cardiac ganglion and increase the rate of the heart beat, giving rise to an increase in the rate of CO<sub>2</sub> production by the nerve-cells of the heart ganglion. The method employed was the same as that previously described by the author. The color change of phenolsulphonephthalein was used to determine the rate of change in hydrogen-ion concentration which resulted from the formation of CO<sub>2</sub> by the excised cardiac ganglion. The ganglionic cord was immersed in 3 c.c. of a standard non-buffer balanced saline solution in small pyrex glass tubes. The initial pH was 7.8, and the time required to reduce the alkalinity to pH 7.4 was used as an index of the rate of CO<sub>2</sub> formation. The standard immersion solution was made by adding 2 c.c. of M/2 Ca Cl<sub>2</sub> to 100 c.c. of M/2 NaCl; the desired initial pH, 7.8, was secured by adding the requisite amount of NaOH. The excised immersed ganglion was stimulated by means of platinum electrodes. The rate of change in the CO<sub>2</sub> production was compared under this treatment with that of the unstimulated ganglion. The tabulated results show that during stimulation the rate of CO<sub>2</sub>

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production is doubled or trebled. This result is unquestionably due to increase in the chemical processes in the nerve-cells; for the faradic stimulation did not produce color changes in the solution, even when the electrodes dipped directly into the solution or were applied to a narcotized ganglion. The decrease in CO<sub>2</sub> production, when the inhibitory nerve to the ganglion was stimulated, served as a control experiment supporting the conclusion that there is a true stimulation of the processes of respiration in the nerve-cells in question. It was also found that the cardiac ganglion could be stretched about 20% of its normal length without injury; under such circumstances the rates of CO<sub>2</sub> production are increased both during and after the stretching operation ceases. Ethyl alcohol in concentrations of 0.5-1.0% by volume, NaCl in isotonic concentration (M/2), adrenalin chlorid 1:10,000, were each found to stimulate the cardiac ganglion of limulus.

With regard to the effect of temperature extremes, it was observed that after exposing the ganglion for five minutes to 0° C. and then again warming to 10° C., the increase in the rate of CO<sub>2</sub> production averaged 28% in 4 experiments. When the ganglia are exposed to the upper extremes of temperature compatible with function, e. g., to 35° or 40° C. and are subsequently cooled, the rate is much slower at the lower temperature than before warming. The results of 4 such experiments indicated a depression in the rate of CO<sub>2</sub> to a point only 78% of the value before exposure to the high temperature.

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**Comparative Studies on Respiration. XIX. A Preliminary Stage in the Progress of Ether Anesthesia.**

*Edith Philip Smith, J. Gen. Physiol., 4:157, Nov. 20, 1921.*

Plants were employed because in such experiments the anesthetic could conveniently be made the only variable. A pure strain of wheat was used, the seeds being germinated in sterile paper cups in a saturated atmosphere in the dark. Contamination by molds was prevented by soaking the dry seeds for ten minutes in full strength hydrogen peroxid before germinating. In the saturated atmosphere the seeds produced an abundance of well-developed root-hairs. The material was used when the roots were from 1-1½ in. long, with abundant surface for absorption and respiration. After being washed in running water the seeds were put into a flask with 100 c.c. distilled water, connected with the respiration apparatus. The average room temperature was 20° C. The indicator used was phenolsulphonephthalein in aqueous solution. The normal rate of respiration was taken as the reciprocal of the time required to change the indicator from pH 7.36 to pH 7.09, these values being chosen as sufficiently different in tint to be easily read. The time varied with the age of the seedlings, ranging between thirty and sixty seconds. The seeds were treated with a watery solution of ether, the concentrations employed being 1%, 3.65% and 7.3% by volume. After the rate of respiration had become constant, 100 c.c. of the required solution was substituted for the distilled water in the flask and the experiment continued. The results are plotted to show that the first effect of ether is to cause a depression in the rate of respiration, followed by a rapid rise above normal, and is succeeded by a fall. With all the concentrations the respiration is ultimately reduced to about the same level; the stronger the ether, the less time is

required to produce this result. Even when the respiration has been reduced below normal, complete recovery is possible on removal from the ether, if sufficient time is allowed.

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**Comparative Studies on Respiration. XX. The Cause of Partial Recovery.**

*O. L. Inman, J. Gen. Physiol., 4:171, Nov. 20, 1921.*

A unicellular alga, chlorella, was isolated from the soil and grown on agar, free from bacteria and other organisms. The agar was added to an aqueous solution of various salts and the whole mixture sterilized in an autoclave. From agar the alga was transferred to a liquid medium prepared in the same manner with the exception that 10 gm. dextrose were used in place of 10 gm. agar. The cultures used in the experiments were grown for a period of thirty days in this liquid medium. The algae were transferred to the respiration chamber together with enough of the medium to make a volume of about 20 c.c. The normal rate of respiration was determined by taking the time necessary for a change from pH 7.78 to pH 7.36. When the normal rate of respiration was practically constant, the algae were separated from the medium by centrifuging. The reagent was then added and measurements of the rate of respiration were made at frequent intervals until the desired point below the normal rate of respiration was reached; the algae were then returned to the normal solution and at intervals the rate of respiration was measured. The results, plotted graphically, show that the respiration of chlorella is diminished by exposure to hypertonic salt solutions and to chloroform. After a short exposure there is complete recovery when the algae are removed to the normal medium. After a longer exposure recovery may be incomplete, as shown by the fact that the rate of respiration fails to rise to the normal level. Staining with methylene blue before and after exposure to these solutions indicated that but few, if any, of the cells were killed as a result of the exposure. This shows that the treatment produces a persistent lowering of the rate of metabolism.

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**On the Action of Certain Substances on Oxygen Consumption.  
V. The Action of Potassium Cyanid in Relation to Respiratory Rate.**

*Albert E. Galigher, Am. J. Physiol., 58:301, Dec. 1, 1921.*

This investigation was undertaken to determine whether exposure to a solution of potassium cyanid of suitable concentration for a given time and under identical conditions will produce a differential effect upon the rate of respiration of parts of organisms of the same species which are similar in structure, but which show considerable differences in rate of respiratory exchange. The experiments were performed upon tissue of *Nereis vexillosa* taken a short distance posterior to the pharynx. After the rate of respiration in sea-water had been determined, the bottles containing the pieces of tissue were filled with a fresh solution of potassium cyanid in sea-water, and the amount of oxygen consumed in a given time was determined, the control bottle also being filled with a quantity of the cyanid solution. The concentration of cyanid used in all of the experiments was 1:5,000 molecular.

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The time of exposure varied in different experiments, but was constant for the three pieces of tissue in any experiment. The tabulated results show that the rate of respiration in *Nereis vexillosa*, as indicated by oxygen consumption, is decreased in the presence of potassium cyanide in the given concentration. The reduction of respiratory rate is greater in regions of the body in which respiration normally proceeds at a high rate than in those of low respiratory activity. The results of this differential action is the partial or total obliteration of the gradient in respiratory rate which has been found to be characteristic of the major axis of this form. The author remarks that since, under similar conditions, axial differentiation is modified in the same manner, the result substantiates the conclusion that the axial metabolic gradients are primary ordering factors in the determination of axiate organization. The data also form further evidence that susceptibility to potassium cyanide may be used as an indicator of metabolic rate, at least of the respiratory processes.

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Guanidin and Dimethylguanidin Toxicosis in Mammals, and Their Physiopathologic Significance.

*E. Frank, R. Stern and M. Nothmann, Ztschr. f. d. ges. exper. Med., 24:341, Berlin, Sept. 22, 1921.*

Creatinin is formed by tonic innervation of the skeletal muscles. The fascicular contractions in frog muscle, known to be caused by guanidin and methylguanidin, originate in the sarcoplasm. Guanidin poisoning was studied in white mice, guinea-pigs, dogs and cats, the cat proving the most satisfactory. Crystallized guanidin hydrochlorate was used, containing 60% of the pure base; 0.20-0.25 gm. per kilo is usually lethal for cats. Symptoms begin with 0.12 gm. At the height of the condition, epileptic attacks often appear, producing loss of consciousness and dyspnea. During the twenty-four hours following poisoning, characteristic slow movements of extension often occur which, during walking, suddenly interrupt flexion of the extended leg; these retrograde contractions are important, because they resemble the "water tremor" which is a characteristic sign of experimental tetany. Comparison of experiments on narcotized and unnarcotized animals showed that the site of the process altering irritability is peripheral, and not spinal. The range between the lethal dose and doses producing no symptoms, as well as changes in galvanic irritability in animals without toxic symptoms, show that there are 2 separate factors in guanidin poisoning, one which causes latent alterations due to the poisoning, the other the stimulus which produces symptoms. By combining guanidin with other substances, the heightened reactivity produced by guanidin poisoning is proved. The cause of the appearances noted in symptomless poisoning may be different in different cases. Endogenous stimulating substances of blood or cells, which are below the threshold of reaction, may cause various symptoms when irritability has been increased. The identity of guanidin poisoning with tetany parathyropriva is confirmed by the fact that in parathyroidectomized dogs, increase of guanidin appears in the urine, and in the blood. A similar increase appeared in the urine of 2 spasmophilic infants.

Dimethylguanidin is about 8 times as toxic as guanidin. Toxic symptoms appear much earlier than with guanidin. The disease-picture is strikingly like spasmophilia in children. The symptomatology of dimethylguanidin poisoning very strongly indicates a relation to similar substances associated with tetany. Guanidins have 2 fundamental properties: (1) They form firm combinations, so that their effects appear gradually. (2) They are not directly irritant, but heighten irritability of certain centers. Tonic contractions of the skeletal muscles produce methylguanidin in the sarcoplasm. The parathyroids prevent undue accumulation of dimethylguanidin in one of the centers, perhaps by giving off a complex to the blood, the latter acting locally on dimethylguanidin formation. Since increased galvanic irritability is connected with diminution of calcium in the tissue-fluids (MacCallum), and since guanidin poison is relieved by administering calcium, it may be stated that guanidin in the tissues is connected with loosening of the calcium-binding influence.

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### Antiketogenesis. III. Calculation of the Ketogenic Balance from the Respiratory Quotient.

*Philip A. Shaffer, J. Biol. Chem., 49:143, Nov., 1921.*

Whenever the rate of production of ketolytic material falls below the rate of the catabolism of ketogenic substances, as happens when the normal subject greatly reduces the carbohydrate intake, and in the diabetic when his power of metabolizing carbohydrate is sufficiently low, there is a deficit of ketolytic substance; in proportion to this deficit, aceto-acetic acid accumulates, is in part converted into acetone and hydroxybutyric acid and is excreted in the three forms as abnormal end products. The author says that, according to this conception, the starvation acidosis of any subject and the often more severe acidosis of diabetes are the result of and are in proportion to the unusual ratio between the rates of the catabolism of ketogenic substances on the one hand and of the formation of the necessary ketolytic substances on the other.

He describes a method of making a calculation of the metabolic mixture and of the ketogenic-antiketogenic balance from the respiratory exchange. Previous workers in this field divided the total metabolism into three fractions: protein, fat and carbohydrate; but Shaffer divides the total somewhat differently, namely, into (a) total glucose (or equivalent antiketogenic substances) including glucose from amino-acids and from glycerol of fat, (b) fatty acid (ketogenic) and (c) the ketogenic fraction of protein. The principle of the calculation is as follows: It is assumed that in the normal subject as well as in the diabetic, glucose (or equivalent substance) is formed from protein to the extent of 3.6 gm. for each gram of nitrogen and as such is to be included in the carbohydrate metabolism. The remainder of the protein, which may be called the non-carbohydrate quota of protein, is assumed to be oxidized parallel with the nitrogen excretion. While the latter assumption is perhaps not always correct, the author believes the error is less than that which results from the assumption that the whole of the protein is concurrently oxidized. The oxygen and carbon dioxid corresponding to the non-carbohydrate quota of pro-

tein are subtracted from the total  $O_2$  and  $CO_2$ ; the remainders represent the oxidation of total glucose (from carbohydrate, protein, and glycerol) and of fatty acid. Their ratio, which is the "fatty acid-total glucose respiratory quotient," interpolated between the theoretical quotients for fatty acid and for glucose shows the relative participation of fatty acid and glucose in the mixture being burned. Finally a correction is made for the ketogenic fraction of protein.

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(1a—64)

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**Variations in Alveolar Carbon Dioxid Pressure in Relation to Meals. A Further Study.**

*E. C. Dodds and T. Izod Bennett, J. Physiol., 55:381, London, Nov. 18, 1921.*

One of the authors has previously shown the changes in alveolar carbon dioxid pressure which follow the ingestion of a meal, namely, a rise of 2-6 mm. in the first half or three-fourths of an hour after the meal, with a subsequent fall below the original level and a return to that level during later stages in digestion. The present experiments were designed to investigate that portion of the curve during which the  $CO_2$  pressure drops below the fasting level. Ryle's modification of the Einhorn duodenal tube was employed for the introduction of food directly into the duodenum. The withdrawal of a small quantity of alkaline bile-stained fluid gives evidence that the tip of the tube has traversed the pylorus and samples of alveolar air are now taken by the Haldane-Priestley method, and analyzed with the Haldane apparatus, an inspiratory and an expiratory sample being taken at each reading, and the mean of the two readings being expressed in mm. Hg. It having been ascertained that the subject's alveolar  $CO_2$  pressure is at a constant level, substances are now introduced through the tube directly into the duodenum by means of a syringe, and the variations in alveolar  $CO_2$  pressure recorded. In the majority of instances oatmeal gruel prepared as for fractional gastric analyses was used. All the experiments showed (a) that the direct introduction of food into the duodenum leads to an immediate fall in alveolar  $CO_2$  pressure with a subsequent return to the fasting level, and (b) that variations in the acidity of the substance introduced do not produce appreciable differences in the response. Gastric lavage with a weak solution of atropin caused an arrest of continuous gastric secretion, and an immediate fall of the fasting level of alveolar  $CO_2$  pressure. Subsequent to gastric lavage with atropin there is no rise in alveolar  $CO_2$  pressure in response to the entry of food into the stomach, but the fall in pressure which follows the passage of food into the duodenum still occurs. Local application of atropin to the duodenal mucosa causes an immediate rise in the fasting level of alveolar  $CO_2$  pressure. After such local application of atropin to the duodenum, no fall of alveolar  $CO_2$  pressure occurs in response to the direct introduction of food into the duodenum, but introduction of food into the stomach evokes the usual rise in pressure with no fall below the fasting level when the food passes beyond the pylorus.

(1a—65)

**Water Storage in the Body. II. Effects of Salt and Sugar Mixtures on the Lymph of the Thoracic Duct in Dogs.**

*Robert Meyer-Bisch, Ztschr. f. d. ges. exper. Med., 24:381, Berlin, Sept. 22, 1921.*

The author has previously shown that marked concentration of the blood in certain cases of tuberculosis, may be so affected by a single injection of tuberculin that an increase in weight is accompanied by decreased concentration of the blood. In a quest for indifferent substances, that might produce the same effect upon the water storage, in the body it was found that intravenous injection of 2 c.c. of a 10% solution of common salt or sugar suppressed profuse perspiration in tuberculous patients for eight days. This effect on water retention was marked, and repetition caused an increase in weight with demonstrable dilution of the blood. The effect, as in tuberculin, appears only after one or two days, showing that it is not due to alterations in osmotic conditions by the small quantity of crystalloids. Altered tissue activity is indicated and should affect the composition of the lymph. Experiments were made on dogs. The lymph of the thoracic duct was studied after injecting small quantities of sugar and salt. The duct was exposed, a metal cannula inserted, lymph was withdrawn every five minutes, the albumin of the separated serum being determined refractometrically and NaCl being estimated by Bangs' method. After injecting 3-10 c.c. of 10% salt solution, the quantity of lymph was at first unchanged, then it decreased; albumin was much diminished, salt increased, independently of the alteration in the water storage, which appeared at the same time. The decrease in the lymph albumin was preceded by a brief increase. The amount of lymph discharged was frequently unaltered or slightly increased, but usually decreased for some time. A second injection had the same effect as the first, showing that the procedure in itself has no influence. Injection of 0.3-1.0 gm. of dextrose, in 10% solution, caused a similar, though weaker result. Intravenous injections of small quantities of dextrose or salt therefore produce retention of water and albumin within the tissues. Injection of larger quantities of salt increases the lymph. By injecting 20 gm. of salt, dissolved in 60 gm. of water, the author determined that there was an increase of lymph, poor in salt but rich in albumin; afterward, increase of lymph rich in salt and still richer in albumin; still later, the amount of lymph was increased, it being rich in salt and poor in albumin, corresponding to the effects of a lymphagogue of the second order. For comparison, an osmotically ineffective substance acting as a lymphagogue of the first order was tried in small quantities, namely, peptone, 0.3-1.0 gm., in 3-10 c.c. water. Retention of albumin and water occurred, indicating that lymphagogues of the first and second orders produce similar effects when used in small quantities. Salt and dextrose therefore affect water storage in tuberculous patients just as tuberculin does.

(1a—66)

**Growth and Foods.**

*G. Mouriquand, P. Michel and L. Barré, Comp. rend. Soc. de biol., 85:865, Paris, Nov. 12, 1921.*

Experiments were made to determine what diet and combination  
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of foods were best for growth. Young pigeons, fed with a single variety of whole grain, survived indefinitely, but their weight remained stationary. Growth was normal on a diet of two varieties of grain. The authors used fowls of the same race and brood, in feeding experiments carried through one hundred days. The diet which showed the greatest daily gain in weight and also the highest coefficient of utilization, was a mixture of fresh grass with bread, bran, and various grains. Barley, wheat and corn, untreated and used with and without grass, gave fair results. Sterilized grains and decorticated rice gave the lowest figures. Fresh barley seems to counteract deficiencies in diet to a notable extent. Birds fed with decorticated rice plus the fresh barley lived indefinitely while those fed on decorticated rice alone lived only thirty-seven days.

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(1a—67)

**Studies in Nutrition. The Choice between Adequate and Inadequate Diet, as Made by Rats and Mice.**

*Helen S. Mitchell and Lafayette B. Mendel, Am. J. Physiol., 58:211, Dec. 1, 1921.*

The object was to determine whether rats and mice would choose or proportion their diets so as to promote normal growth when given a choice between two "synthetic" food mixtures differing only in the type or amount of a single constituent. Observations were also made on the ability of rats to select an adequate diet when a choice of natural foods was offered. To lessen the number of factors involved, most of the experiments offered only two possibilities of choice to an animal; an attempt was made to keep the consistency and appearance of the two foods as nearly alike as possible. The types of choice offered in the form of "synthetic" paste foods were as follows: (1) High and low content of protein. (2) "Complete" and "incomplete" protein (foods containing casein vs. zein). (3) High and low content of vitamin A. (4) High and low content of vitamin B. (5) High and low content of inorganic salts. In the experiment offering a choice of natural foods, only rats were used and they were offered a choice between ground whole corn and dry meat meal and, in addition, were allowed free access to the salt mixture such as was used in the "synthetic" food mixtures. In all the experiments the animals were weighed twice a week and foods once a week. The authors report that the investigation shows in general that rats and mice in their choices of foods, make selections which are as a rule advantageous for their nutritive condition. This was true even in the choice between "synthetic" mixtures which appear to the senses essentially alike. The choices made tended to promote normal growth in the young and maintenance in the adult although the proportions of the foods eaten varied with the individual.

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**Nutrition of Children and Adolescents from Two to Twenty Years of Age.**

*Jules Renault and C. de Tannenberg, Presse méd., 29:977, Paris, Dec. 10, 1921.*

The diets recommended are not based upon theoretic considerations but on the observation of the actual amount of food freely  
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taken by healthy children and young men. These amounts are somewhat greater than those usually recommended by French authors. This is in general agreement with the observations of Gephart in America who found that school boys on an average take quantities of food equivalent to 5,000 calories per day, which is nearly twice the amount of an average adult ration. Anemia coincides frequently with an insufficient consumption of meat. Although in the light of present knowledge it cannot be said that such a diet produces anemia, it does seem to keep it up and to aggravate it, while a flesh diet usually improves this condition. It is better to give children an excess of nitrogenous food rather than to limit them to a strict minimum, and albumins of animal origin should make up at least 50% of the total nitrogenous foods supplied.

The average proportions between the various elements of the diet were found to be as follows: fats 1 part, albumins 2, carbohydrates 4-8, according to age. From 2 to 4 years the proportion of fats was higher (fats 1, albumins 1.1, carbohydrates 3.7.) Practically it is advisable to increase the amount of fats in cold weather or in order to meet the requirements produced by a greater outlay of energy. Albumins and meat especially should be increased when children grow rapidly or are anemic. Although the added food requirements produced by work in adults have been worked out, next to nothing is known as to those of children. In the age rations which have been prepared, this element has been taken into account from the actual observation of healthy children, who play or exercise normally. A curve representing the number of calories required per kilo of body weight, shows a maximum rise at the age of 2. It declines thereafter steadily, being interrupted by slight elevations at the ages of 8 and 12. During the period of puberty the decline is slight, and much more rapid in the adult. The curve representing the number of calories required per day shows on the contrary a continuous rise, except during the period from 8 to 12. It declines rapidly after the age of 30. No special attention has been given in this study to vitamins, as they are adequately supplied in a varied diet containing fresh vegetables, fruits and butter. The data of course represent only averages and great individual variations exist in different children.

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(1a—69)

**The Nutritive Value of Beer.**

*H. Kionka, Deutsch. med. Wochenschr., 47:1288, Berlin, Oct. 27, 1921.*

The total value of beer is determined by the percentages of alcohol and of free carbon dioxid, the viscosity, the characteristic taste, and the appearance. (1) The alcohol present, to the extent of about 3%, does not induce rapid intoxication. The influence on the circulatory system of large quantities of liquid may cause the so-called "beer heart." This malady, however, is not solely due to the consumption of excessive quantities of fluids, at all events so long as the kidneys are functioning normally. If these organs are diseased, serious derangement of the circulatory system will result. The author believes that the calcium content of beer (34% of the ash) may, in the course of time, by

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gradual absorption or heavy drinking, increase the percentage of calcium in the blood. In cases of the least abnormality in the kidney secretions, an increase of calcium in the blood will adversely affect the muscles of the heart. Beers, other than the Munich-brewed, and containing much smaller percentages of calcium, do not cause any disturbance of the heart's action. (2) Carbon dioxid occurs normally to the extent of 0.350.4%, and in beers more heavily charged, up to as much as 0.7%. The action of the gas is chiefly confined to improving the taste of the beer. (3) Viscosity depends, in great measure, on the percentage of CO<sub>2</sub>. Beers which do not foam or have no "head," taste flat. The activity of the isolated bubbles of CO<sub>2</sub> in beers is modified by the colloids with which they are surrounded. Foam formation is dependent on the percentage of albuminous matter present, and the capacity to retain the foam or "head" is regulated by the presence of carbohydrates, especially those of dextrinous nature. (4) Beers have no standard taste, by reason of the varying quantities, in different samples of a great variety of saccharids, salts and bitter principles. Further, the flavor of beer is determined by the type of water used in brewing. Beers should be quite free from unpleasant taste. (5) The appearance is judged by its even color, clearness, freedom from glutin-cloudiness (caused by variations of temperature), and the absence of budding yeasts or bacteria in active development.

In conjunction with its alcohol and CO<sub>2</sub> contents, it is the colloids which determine the nutritive value of beer.

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**Energy Expenditure during Walking, Expressed in Calories.**

*A. Waller and G. de Decker, Compt. rend. Soc. de biol., 85:853, Paris, Nov. 12, 1921.*

Results were obtained by the usual method (measurement of carbon dioxid and oxygen, to obtain the respiratory quotient) and by the method of using only carbon dioxid, the number of c.c. of carbon dioxid being multiplied by the factor 5.333; or 1 c.c. of carbon dioxid per second is taken as equal to 20 kilocalories per hour. Two series of observations are tabulated. The first series showed expenditure of 3.4 c.c. carbon dioxid per second, during repose and a mean expenditure of 15.8 c.c. during walking, the net expenditure being 12.4 c.c. carbon dioxid per second. The corresponding figures for the second series were 3.4, 16.8 and (net) 13.4 c.c. carbon dioxid per second. The subject weighed 52 kilos and walked at a speed of 6 kilometers per hour, or 1.67 meters per second. The work per second was 86.84 horizontal kilogrammeters. The expenditure of carbon dioxid per horizontal kilogrammeter for first series was 12.4 divided by 86.84, or 0.1428 c.c.; for the second series, 13.4 divided by 86.84, or 0.1543 c.c. The similarity of results is also shown by assigning a mean value of 0.9 to the respiratory quotient, the analytical temperature being 16.5° the result is equivalent to 1 c.c. carbon dioxid per second, or 20 kilocalories per hour.

## 1b. BIOLOGIC AND ORGANIC CHEMISTRY

(1b—1)

(1b—1)

The Significance of Acid Production by Bacteria in Some Problems of Physiologic Chemistry.

*Ernst Seitz, Ztschr. f. d. ges. exper. Med., 25:66, Berlin, Oct. 14, 1921.*

The behavior of various bacteria to certain sugars is a means for their differentiation. This characteristic might possibly serve the opposite purpose, that of determining the variety of sugar present in organic fluids by their fermentative reactions with certain bacteria. It would thus be possible to separate different sugars in serum. In suitable cases, the quantity of sugar could be determined bacteriologically by titration of the acid formed. This presupposes the neutralization of alkali produced by bacterial growth, and the medium must contain as little albumin as possible to assure exact titration. Attempts to determine the sugars in blood-serum have so far been unsuccessful, for the removal of the albumin with acetic acid causes a splitting of the albumin with acid production. Better results might possibly be obtained by using a Bechold filter.

The author has studied the carbohydrates of milk by the bacteriologic method. The casein was precipitated with acetic acid, the filtered whey was sterilized and inoculated with *B. typhosus*. Within twenty-four hours acid was produced. In an aqueous solution of lactose of the same concentration inoculated with the same bacterium, adding disodium phosphate as nutrient material and litmus as an indicator, acid was produced in twenty-four hours, but in much smaller quantity, the same amount of acid was formed in a solution of phosphate and litmus containing no lactose. As all traces of agar medium had been removed from the culture by washing, the small amount of acid might be due to traces of organic material in the distilled water, or to a product of bacterial metabolism (the latter seems more probable). The more abundant acid production in whey might be attributed to the presence of decomposition products of lactose, formed during sterilization; but the acid was also formed when the whey was sterilized by filtration through a Berkefeld filter. Proteins were ruled out as a source of the acid by the complete removal of albumin. The author assumed that another carbohydrate besides lactose was present in milk, and that it behaved like dextrose. This same carbohydrate is found in human milk. The assumption that it was dextrose (diffused from the blood into the milk) is supported by the fact that the acid formation by *Bacillus typhosus* varied directly with the amount of sugar in the blood.

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A Buffer Solution for Colorimetric Comparison.

*T. C. McIlvaine, J. Biol. Chem., 49:183, Nov., 1921.*

The author has developed a system requiring but two stock buffer solutions for colorimetric comparison. These solutions cover a range of from pH 2.2 to pH 8.0 which includes approximately the limits of reaction for arable soils and physiological media. The materials used are: 0.2 M disodium phosphate and 0.1 M citric acid, combined in such volumes as to make 20 c.c. of the mixture. The disodium phosphate employed was recrystallized 3 times. The citric acid was recrystallized at  
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least twice before using. The 0.2 M disodium phosphate solution was prepared by titration against HCl, using methyl orange as indicator. The 0.1 M stock solution of citric acid was standardized by titration against NaOH solution which had been prepared with boiled water and protected from carbon dioxid. The correct weight of citric acid required to make the stock solution can also be determined by titration. The pH values of the mixtures were determined electrometrically by the use of the chain: Hg HgCl nKCl saturated solution of KCl H<sub>2</sub> Pt. No allowance was made for liquid potential. No attempt was made to maintain a constant temperature but the temperature of both calomel electrode and buffer solution were taken into account by the author in computing the pH values. Clark's extension of Sorensen's values for the normal calomel electrodes was employed with the necessary interpolations. Three extra calomel electrodes were used for checking the accuracy of the one in general use. A Leeds and Northrup type K potentiometer and type R sensitive *galvanometer* were used for making the electrometric measurements. The electrode was of the platinum wire variety. The hydrogen was generated electrolytically and passed first through an acid permanganate solution, next through a hot tube, and finally through a wash bottle containing distilled water. The author constructed a graph in which the pH values (determined electrometrically) of various mixtures of phosphate and citric acid solution (total volume in all cases 20 c.c.) were plotted against the volumes of the 2 solutions. By interpolation, using the curve so obtained, it was possible to arrive at the proper volumes of the 2 solutions which when mixed would give 20 c.c. of a solution having any desired reaction. The tabulated values given in the article were obtained in this way and checked by actually preparing the solutions and measuring the pH values by the electrometric method. In all cases the variation of the observed from the calculated pH was 0.01 or less.

(1b-3)

The Chemical Composition of the Ovaries of Fresh-Water Gar,  
*Lepidosteus*.

*Erwin E. Nelson and Charles W. Greene, J. Biol. Chem., 49:47, Nov., 1921.*

The authors obtained samples of gar ovary from twelve specimens of *Lepidosteus platostomus* and one sample of *Lepidosteus osseus*. The samples of tissue for analysis were in all cases taken fresh, generally while still physiologically alive. Samples of the ovaries were placed in weighed glass-stoppered bottles, weighed promptly and transferred to casseroles, and, extraction with hot alcohol was begun at once; or they were covered with 95% alcohol and sealed with hard paraffin for transportation. Samples for the determination of water were taken at the same time and weighed at once, then dried to constant weight at 105° C. The authors determined the amount of lipoids, proteins, organic extractives and inorganic ash and water present in the samples examined; the results were tabulated in terms of parts per 100 gm. of moist sample. These results show that, broadly speaking, the protein, except in the very young, remains comparatively constant. The organic extractives are also constant. The total lipoids tend to increase and the total water to decrease with development of the gar ovaries. The authors were not successful in securing ripe ova for analysis.

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**The Chemical Composition of the Skeletal Muscle of the Fresh-Water Gar, Lepidosteus.**

*Charles W. Greene and Erwin E. Nelson, J. Biol. Chem., 49:57, Nov., 1921.*

The results are tabulated in terms of parts per 100 gm. of moist sample and are as follows: Lipoids from 2.23 to 13.19; protein from 13.52 to 15.17; organic extractives from 2.59 to 4.61; ash from 0.43 to 1.33; total N from 0.30 to 0.51; amino N from 0.064 to 0.094; creatin from 0.21 to 0.30; water, by difference from 66.4 to 79.7; water, by determination from 71.7 to 79.5. The authors remark that the preceding analyses show that the gar flesh compares favorably with that of those species which contain the moderate amounts of stored lipoids and that on the whole it is a very palatable food of good caloric value.

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(1b—5)

**Del Rio-Hortega's Method of Impregnation Applied to a Study of the Pigment of Crustaceans.**

*J. Verne, Compt. rend. Soc. de biol., 85:806, Paris, Nov. 5, 1921.*

The original method consists of impregnating frozen sections with ammoniacal silver carbonate. The author applied the method to the subcutaneous tissues of crustaceans, which is too delicate to permit freezing. The tissue was spread on a slide and fixed for from fifteen to twenty minutes in 10% formol; it was then detached from the slide, rapidly washed and impregnated for from thirty to forty seconds in ammoniacal silver carbonate, reduced in 1% formol for some minutes and passed through gold. The time indicated for the several phases must be strictly observed. His results coincide with those of Del Rio-Hortega. The pigment cells of crustaceans have the same appearance as the cells described by the latter as producing melanophores in human skin. The author considers that a prepigmentary substance, which he calls pigment amino-acid, produces melanin by fermentative oxidation. The appearance of the stellate cells depends on the time they are kept in the silver solution; the contents of the cells may appear finely granular, very finely stippled or almost homogeneous. The pigment is dissolved by too prolonged exposure to formol or silver carbonate. Melanophores are never found without chromatophores which are argentophil, but do not show melanin. In the absence of melanin, chromatophores occur alone. This condition is described by Del Rio in unpigmented human skin, most common in the white race; the author finds it in the lower layer of the subcutaneous tissue in certain crustaceans. There is marked analogy between the author's amino-acidophores and the cells described by Del Rio as preceding melanophores. Variations in the affinity for the silver may be characteristic of disintegration of proteins, especially those from which melanin originates.

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(1b—6)

**The Origin of the Potential Differences Responsible for Anomalous Osmosis.**

*Jacques Loeb, J. Gen. Physiol., 4:213, Nov. 20, 1921.*

Collodion bags coated with gelatin on the inside were filled with a M/256 solution of neutral salt (e. g., NaCl, CaCl<sub>2</sub>, CeCl<sub>3</sub>, or Na<sub>2</sub>SO<sub>4</sub>) (Sec. 1—Page 51)

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made up in various concentrations of  $\text{HNO}_3$  (varying from N/50,000 to N/100). Each collodion bag was put into an  $\text{HNO}_3$  solution of the same concentration as that inside the bag but containing no salt. In this case water diffuses from the outside solution (containing no salt) into the inside solution (containing the salt) with a relative initial velocity which can be expressed by the following rules: (a) Water diffuses into the salt solution as if the particles of water were negatively charged and as if they were attracted by the cation and repelled by the anion of the salt with a force increasing with the valence of the ion. (b) The initial rate of the diffusion of water is a minimum at the hydrogen ion concentration of about N/50,000 HCl (pH 4.7, which is the point at which gelatin is not ionized), rises with increasing hydrogen ion concentration until it reaches a maximum, and then diminishes again with a further rise in the initial hydrogen-ion concentration. The potential differences between the salt solution and the outside solution (originally free from salt) were measured after the diffusion had been going on for one hour; when these values were plotted as ordinates over the original pH as abscissae, the curves obtained were found to be similar to the osmotic rate curves. This confirmed the view expressed by previous authors that these cases of anomalous osmosis are in reality cases of electric endosmose, where the driving force is a potential difference between the opposite sides of the membrane.

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(1b-7)

**Exosmosis from Animal Cells.**

*J. Gray, J. Physiol., 55:322, London, Nov. 18, 1921.*

Gray has previously shown that when living trout eggs are injured there is a very marked evolution of electrolytes to any medium whose concentration of intracellular electrolytes is less than that of the interior of the egg, also that the mechanism whereby healthy eggs retain their electrolytes must lie in the protoplasmic membrane. The only satisfactory way of measuring the rate at which electrolytes leave a cell is to estimate (by electric or other means) their concentration in the surrounding medium at various stages of the reaction. Such experiments have been performed by previous workers with complete tissues or with a large number of cells. But the rate of exosmosis from a cell can be studied only by the use of single cells. By means of a special apparatus illustrated in the article Gray accomplishes this, the exosmosis being measured by determining the electric conductivity of the external medium. A large number of experiments, the results of which are recorded graphically, show that the absolute rate of exosmosis from different eggs in the same solution is simply an index of the susceptibility of the different cells. They also show that the general nature of exosmosis is the same in all cases. There is an initial phase during which the cell membrane is destroyed; the length of this phase depends upon (a) the resistance of the individual cell, and (b) the strength of the toxic solution. Once this initial phase is over, the electrolytes diffuse out of the cell according to simple diffusion laws. There is no evidence to support the view that the intracellular electrolytes represent the equilibrium of such a system as is postulated by Donnan or by Moore.

(1b-7)

(1b-8)

**The Hydrogen-Ion Concentration of the Aqueous Humor of Fetuses of Various Ages.**

*J. W. Nordenson, Upsala Läkaref. Förh. 36, No. 25, Stockholm, Sept. 1, 1921.*

The author has determined the hydrogen-ion concentration of the aqueous humor of fetuses at different stages of development. He employed Felton's colorimetric method in the determinations and performed his experiments on the eyes of a series of cows and calf fetuses of various ages. The eyes were obtained from the communal slaughter house in Stockholm immediately after the killing of the animals. The temperature during the determinations was between 16° and 18° C. The results showed that the hydrogen-ion concentration of the humor of cows is somewhat lower (average 7.67) than of calf fetuses (7.72). In 12 fetuses the figure was higher than in cows; in 3 cases the figure was the same for both, and in 5 cows it was higher than in the fetuses. No difference in the hydrogen-ion concentration could be observed between fetuses of various ages. No important changes in the hydrogen-ion concentration occur during fetal life. However, the concentration is somewhat higher during fetal life than after birth.

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(1b-9)

**Chemical Condition Necessary for the Retention of Normal Cell-Structure. IV. The Difference in Volume of Water and Nitrogen in Muscle Treated with Sodium Chlorid and Calcium Chlorid.**

*E. M. P. Widmark and G. Lindahl, Skandinav. Arch. f. Physiol., 41:221, Leipzig, Sept., 1921.*

About ten years ago Widmark described the peculiar action of calcium, barium and strontium salts on muscle tissue. In these tests the salts were embodied in the muscle cells by cutting up the muscle into pulp with scissors, so that the cells no longer impeded infiltration. The loss of weight of the muscle tissue in different solutions was registered as follows: The tissue, after preparation, was placed upon a piece of gauze and the excess moisture was removed by slight pressure between sheets of filter paper. The tissue was then weighed, the shrinkage being determined by the difference in weight of muscle treated with sodium chlorid solution and with alkaline earth solutions. In all these tests the freezing-point of the solutions was approximated by the addition of sodium chlorid to the freezing-point of the blood of the animals from which the muscle tissue was derived.

In making these former tests it was assumed that the reduction in weight took place in two ways: (a) Salts of alkaline earths extract albumin from muscle tissue. The loss of weight is due to the loss of dissolved albumin. (b) The salts cause dehydration of muscle albumin. The loss of weight is due to the loss of water.

In the first case the water content of muscle tissue should remain practically unchanged after treatment with salt, and the amount of nitrogen in the salt solution should increase. In the second case the water content should diminish, while the amount of nitrogen in solution should have a higher value than in the control.

The experiments tended to show that the second case conforms with the results, although a slight dissolution of albumin cannot be denied. A certain amount of muscle tissue (5 gm.) was treated with

sodium chlorid and calcium chlorid for comparison. The muscle treated with sodium chlorid did not shrink but increased in weight, while that treated with calcium chlorid lost weight. Muscle tissue treated with calcium chlorid contains less water than that treated with sodium chlorid (3.587 against 4.419 gm.) The dry substance is almost the same in both groups (0.892 with  $\text{CaCl}_2$ , against 0.908 gm. with  $\text{NaCl}$ ). The decrease in weight through shrinkage is really due to a loss of water. The amount of nitrogen given up to the solution during the process of shrinkage is, on an average, 38.45 gm. with  $\text{CaCl}_2$  and 35.85 gm. with  $\text{NaCl}$ . The loss of weight during shrinkage is due to the action of the calcium chlorid ions on muscle tissue and is to be sought in the loss of water exclusively. Dehydration of muscle colloid is the most probable explanation.

(1b—10)

(1b—10)

**The Selective Absorption of Potassium by Animal Cells. II. The Cause of Potassium Selection as Indicated by the Absorption of Rubidium and Cesium.**

*Philip H. Mitchell, J. Walter Wilson and Ralph E. Stanton, J. Gen. Physiol., 4:141, Nov. 20, 1921.*

In their experiments the authors perfused frog muscles with a Ringer solution modified by the replacement of potassium chlorid with an equimolar concentration of rubidium chlorid. While both legs were perfused the muscles of one were made to contract by stimulation of the lumbar plexus with maximal tetanizing induction shocks lasting one second, at thirty second intervals, during one-half hour periods with alternating one-half hour periods of complete rest. In one experiment this procedure was continued during five hours and was followed by perfusion with an isotonic cane sugar solution during one and one-half hours. All the muscles of both legs showed irritability at the end of the experiment. Samples of the gastrocnemius and sartorius muscles of each leg were decomposed in a mixture of nitric and sulphuric acids. In the resulting solutions rubidium could be detected spectroscopically only in the muscles of the stimulated leg. In another similar experiment the muscles of one leg were given 540 contractions of one second each, and were then, while resting, perfused during two hours with a potassium-free Ringer solution. The muscles of both legs showed good irritability at the end of the experiment. The wet-ashed muscle samples, taken from the gastrocnemius and vastus muscles of each leg, were examined for rubidium. No trace of rubidium could be detected in the muscles perfused without stimulation, but in the muscles of the stimulated legs approximately 0.011% rubidium was found. Similar experiments were made with cesium chlorid, replacing, in equimolar concentration, the potassium chlorid of Ringer solution. The tabulated results show that cesium, like rubidium, was taken into the muscle substance so as to be retained, in part, during the subsequent perfusion with potassium-free Ringer solution. Retention of cesium by a resting muscle did not occur.

Rats on synthetic diets, adequate in all respects except that potassium was replaced by an equivalent amount of rubidium or cesium, died after a period varying from 10 to 17 days with characteristic symptoms including tetanic spasms. Muscle, heart, liver, kidney, spleen, and lung tissues were then found to contain significant amounts of rubidium or cesium. The concentration of these metals in the muscle amounted, in

some cases, as shown by a spectroscopic estimation, to about half the concentration of potassium normally found in mammalian muscle. The results tend to confirm the theory that the peculiarities in the physiologic effects of potassium, including the facility with which it is selected by living cells in preference to sodium, are related to the electronic structure of the potassium ion as compared with that of similar ions. The possible relationship of the comparative migration velocity, a function of the electronic structure, to physiologic effects is suggested.

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(1b-11)

**Calcium Content of the Cerebrospinal Fluid.**

*R. Kummer and G. Minkoff, Compt. rend. Soc. de biol., 85:864, Paris, Nov. 12, 1921.*

The authors have failed to find anything in the literature on this subject. They examined the cerebrospinal fluid of 4 normal subjects by Kramer and Tisdall's method. The quantity of calcium stated in parts per 1000, determined by them for each subject, was 0.050, 0.050, 0.050 and 0.052. Further research confirms the average normal of 0.05 parts per 1000. The content of the blood varies between 0.08 and 0.12 per 1000.

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(1b-12)

**Studies on Succinohydrogenate.**

*E. M. P. Widmark, Skandinav. Arch. f. Physiol., 41:200, Berlin, Sept., 1921.*

According to the studies of Batelli and Stern the tissue substance which influences the oxidation of succinic acid is an enzyme with an optimum of temperature lying between 40° and 50° C, but which is destroyed by slowly increasing the temperature to 60° for fifteen minutes. It is possible to isolate it by mixing finely ground organic tissue with one-third its volume of slightly alkaline H<sub>2</sub>O. In the tests described, the solution of enzyme (dehydrogenated) was prepared of ground horse or ox muscle-tissue. It was then washed clean of blood and centrifuged with 5 times its volume of a 1.5% solution of sodium for one hour. After centrifugalization the opalescent film is poured off and filtered. The extract will keep well if toluol is added. Further attempts to purify the enzyme failed. Precipitation with alcohol and acetone are ineffective.

Experiments to ascertain the influence of the amount of enzyme on the process of decolorization of the system containing succinic acid enzyme and methylene-blue were conducted so that the amounts of fluid, succinic acid and methylene-blue were kept constant, and only the concentration of enzyme was varied. Numerous tests justify the conclusion that the power of decolorization is directly proportional to concentration of the enzyme. Further tests of the dependence of the power of decolorization upon the concentration of the succinate, where this alone was increased, showed that, when enzyme and methylene-blue concentration remained constant, decolorization is stimulated on increased concentration of the succinate, and asymptotically approaches a certain valuation. As regards the relation between the time necessary for decolorization and the concentration of methylene-blue the tests proved that, where only the methylene-blue concentration was increased, no conclusions could be drawn from the faculty of decolorization with varying concentrations of methylene-blue. Conclusions may be possible when we have more

thoroughly studied the nature of a white, flaky precipitate which increases in amount proportional to the amount of methylene-blue used. It is possible that the production of this precipitate is related to the property that some dyes have of precipitating albumin.

(1b—13)

**The Location of Peroxidase in the Cell and its Presence in Sexual Cells.**

*M. Prenant, Compt. rend. Soc. de biol., 85:808, Paris, Nov. 5, 1921.*

The author's studies with benzidin and  $H_2O_2$  on cytologic peroxidase prove that the latter is found only in the cytoplasm. Blue staining of the nucleus is unusual, and may always be imputed to hemoglobin, which gives the same reaction as do the oxidases. When cytoplasm oxidizes benzidin in the presence of hydrogen peroxid, and this action is not due to hemoglobin, the reaction affects only bodies which are analogous to pigment granules or mitochondria. The author describes mitoses which correspond to descriptions by Gatenby and others. This is the first time that a diastase, admittedly present in certain mitochondria, has been demonstrated microchemically. The author has proved the same for 11 varieties of Pulmonata. They suggest that the spermatozoid may contain oxidizing ferments which are absent in the ovum. In 28 species of mollusks and gasteropods examined, the author has not been able to stain the chondriosome at any stage of spermatogenesis. But in lamellibranch and prosobranch gasteropods studied by the author, numerous mitochondrial granulations, sometimes grouped into a kind of accessory nucleus, stain blue. If an oxidizing ferment, essential to fecundation, is absent from the ovum, it is not identical with the peroxidase observed. After fecundation, in Pulmonata, mitochondria brought to the ovum by the sperm no longer stain, whether because the peroxidase has disappeared or because it is inhibited by the ovum, is not clear. In lamellibranch and prosobranch organisms, the mitochondria of the ovum still stain; in *Purpura lapillus* L., they stain up to the thirty-second stage of segmentation. If staining does not occur in the mitochondria of the spermatozoa, in consequence of the changed environment, this may possibly afford a means of studying them separately.

(1b—14)

**Critical Remarks as to the Method of Determining Reducing Substances in the Tissues.**

*Wilhelm Geschwind, Uppsala Läkaref. Förh., 36, No. 10, Stockholm, Sept. 1, 1921.*

If freshly prepared solutions of iron chlorid and potassium ferrocyanid are mixed, a brown solution is obtained; later a dark green precipitate is formed. This substance is called Berlin blue (Iron ferricyanid). Some authors have employed this method for determining reducing substances in the tissues. The author claims that the chemic process of the staining test has been interpreted erroneously and that the results obtained by means of the test are therefore also erroneous.

If a piece of skin is stained with the brown solution (1% dilution of the mixture of iron chlorid and potassium ferrocyanid) the epidermis—except the basal horny layer and the root-sheath—is stained dark green. Also the glandular element of the skin becomes stained dark green, but the connective tissue in the subcutis becomes light green or

(1b—13)

yellowish green. The basal horny layer and the root-sheath, together with the nuclei, are not stained at all, or become light yellow or yellowish green. The 1% solution of  $K_3Fe(CN)_6$  is about  $\frac{N}{10}(\frac{N}{10} = 1.1\%)$ ; the 1% solution of  $FeCl_3$  is almost  $\frac{N}{5}$  ( $= 0.6\%$ ). The mixture of these solutions contains, besides iron ferrocyanid, also free HCl and  $K_3Fe(CN)_6$ . It can therefore be presumed that the dark green shading of the tissue elements is analogous to the staining of gelatin with the iron ferrocyanid, and that the yellow color depends upon the surplus of  $K_3Fe(CN)_6$ . The author has performed several experiments which have confirmed his theory. The histochemical conclusions of Unna-Colodetz, concerning the reducing power of the iron ferrocyanid solution, or rather the acidity and alkalescence, must therefore be considered uncertain.

(1b—15)

**The Formation of Carbohydrates in Striated Muscle.**

*Fritz Laquer, Hoppe-Seyler's Ztschr. f. Physiol. Chem., 116:169, Berlin, Sept. 26, 1921.*

Muscle extract of warm-blooded animals yields lactic acid at  $40^\circ$ , and the formation can be retarded by addition of acid, and considerably advanced by addition of bicarbonate. The lactic acid which the muscle can form from its own component parts under the conditions considered as the best is called genuine lactic acid, while that which results from the substances added is additional formation of lactic acid. The lactic acid existing without neutralization is termed actual maximum of acid formation, and that which is obtainable under the influence of added substances is potential maximum of acid formation. Frogs were killed and the hind-legs skinned; some were used to determine the glycogen contents of the undestroyed muscles, while others in the form of a pulp were distributed in weighing-tubes and exposed at the desired temperature to autolysis for three hours. The trial was interrupted by HCl and the precipitation of the albumin by means of saturated solution of sublimate completed according to the Schenck method. The filtrate was freed of mercury by means of  $H_2S$ , and used to determine the lactic acid. This determination was made by means of extractions by ether in a micro-extraction apparatus. The prepared solution of lactic acid is oxidized by means of a N/250 solution of potassium permanganate, distilled, and the volumetric decrease of a bisulphite solution compared with an N/50 iodin solution determined. Each cubic centimeter of iodin solution consumed corresponds to 0.9 microgram lactic acid. The determination of the glycogen was made in conformity with the abbreviated Pfüger method. The addition of different substances to the muscle pulp, and their influence on the formation of the lactic acid were examined on the basis of theoretic considerations; potassium phosphate, potassium cyanid, glycogen and grape-sugar were tested; determinations were made of lactic acid in the muscle pulp of frogs in winter and in spring, without the addition of carbohydrate, and with grape-sugar, with glycogen and with maltose in potassium bicarbonate, and in sodium and potassium phosphate. Also time tests at  $30^\circ$  and  $45^\circ$  were made and the results tabulated to show the following:

By means of the micro-ether-extraction method, 2-10 micrograms lactic acid could be obtained. Solution of phosphate containing 1.45% (Sec. 1—Page 57)

$H_3PO_4$  produces the best conditions for formation of lactic acid, but at  $30^\circ$  and at  $45^\circ$ , there are characteristic differences in the curves. The lactic acid formed as a rule exceed the original glycogen content. In spring and summer frogs, the lactic acid values correspond to the contents of glycogen and lactacidogen. In winter frogs, the values of lactic acid exceed the sum of the other two, which indicates that in addition to these two substances there are still other as yet unknown carbohydrates in muscle, which can be designated as intermediate carbohydrates. At  $45^\circ$  there appeared additional glycogen and vegetable starch and phosphate of hexose as strong formers of lactic acid, while no lactic acid resulted from maltose, dextrose and levulose. Winter frogs which have been exposed for several days to the incubator temperature of  $22-27^\circ$  regain the capacity which they had lost of forming lactic acid from added glycogen. The active participation of the phosphate in the formation of the carbohydrate is apparent from the fact that additional glycogen is changed into lactic acid only in the phosphate solution and not in the bicarbonate solution.

At  $30^\circ$ , glycogen, dextrose and levulose also formed lactic acid, which shows that grape-sugar and fruit-sugar, contrary to the case with glycogen and lactacidogen, are employed in muscle, not directly, but only after it has changed them to a more easily available form. This ability of the muscle to change grape-sugar into a form more easily available can easily be impaired. This fact may explain diabetic disturbances in assimilation. Potassium cyanid is without influence on the formation of lactic acid from added glycogen.

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**Insaponifiable Tissue Substances Other Than Cholesterin.**

*P. Lemland, Compt. rend. Soc. de biol., 85:839, Paris, Nov. 12, 1921.*

The author briefly reviews previous determinations. He has endeavored to make estimates (not including cholesterin) of fats and lipoids in the liver, kidney, lung and muscle, of normal rabbits. His tabulated results show that insaponifiable fats and lipoids exist in the tissues studied often in greater quantities than that of cholesterin. It was necessary to modify the usual methods. The author's process will be given later.

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**The Influence of Electrolytes on the Solution and Precipitation of Casein and Gelatin.**

*Jacques Loeb and Robert F. Loeb, J. Gen. Physiol., 4:187, Nov. 20, 1921.*

Colloids may be divided into 2 groups according to the ease with which their solutions or suspensions may be precipitated by electrolytes. One group, hydrophilic colloids, (e. g., solutions of gelatin or crystalline egg-albumin in water) requires high concentrations of electrolytes for this purpose, while the other group, hydrophobic colloids, requires low concentrations. In the latter group the precipitating ion of the salt has the opposite sign of charge as the colloidal particle, while no such relation exists in the precipitation of colloids of the first group. One per cent. solutions of casein chlorid of pH 2.2 were prepared in different concentrations of salts in water of about the same pH. That concen-

tration was determined which causes an almost instantaneous complete precipitation of the originally milky solution, so that the supernatant liquid became as clear as water. The solution of the casein in chlorid depends on forces regulated by the Donnan equilibrium. This was shown to be the case by microscopic observation of the mechanism of the solution of solid particles of originally isolectric casein in solutions of acids of different concentration. The particles of casein swell in a solution of HCl, becoming more and more transparent the more they swell; when the swelling reaches a certain stage the particles disappear. The swelling of casein particles appears to be a necessary prerequisite for the solution of casein-acid salts, since such particles are dissolved only when their swelling exceeds a definite limit.

For the precipitation of solutions of gelatin in water, enormous concentrations of salts are required. It is probable that the forces causing solution are the forces of residual valency. Solutions of gelatin are always more readily salted out by sulphates than by chlorids, regardless of the pH of the gelatin solution, thus showing that Donnan equilibrium is not concerned.

(1b-18)

**Influence of Reaction on the Action of Trypsin.**

*W. E. Ringer, Hoppe-Seyler's Ztschr. f. Physiol. Chem., 116:107, Berlin, Sept. 26, 1921.*

Examinations were made in order to verify the results of Michaelis-Davidsohn, Palitzsch-Walbom and Meyer, with reference to trypsin, which is supposed to be a nucleoproteid with iso-electrical point pH = 3.7-4.0, and flocculation optimum pH = 3.59. The trypsin was made to act on fibrin and dissolved albumin. A pancreas extract activated with enterokinase was used as enzyme. In order to measure the action of the trypsin, the fibrin was colored with an alcoholic blue solution, and the color of the liquid deepened with a few drops of hydrochloric acid. The H-ion concentration was determined electrometrically with very small electrodes at 18° and the digestion trials carried out at 37°. The series of trials were carried out (30 mg. trypsin, 6.24 c.c. borate with 5.76 c.c. decinormal hydrochloric acid) with activated enzyme and with enzyme inactivated at 78° and later with 7.52 c.c. glycocoll solution and 0.54 c.c. decinormal sodium hydroxid solution. No true optimum reaction was found. The action of the trypsin became stronger the more alkaline the reaction was, until a limit was set to it by destruction of the trypsin. By this method, an optimum action was obtained at pH = 11.3 at 37°.

The trypsin destruction was tested in hydrochloric acid (0.0557 normal), acetic acid (0.184 normal) sodium chlorid (0.154 normal) glycocoll and NaOH (0.1 normal) in different dilutions, furthermore, with a dialyzed serum, and extracted fibrin, and it was found that the trypsin can be conserved at a not very high acid reaction pH = 3.15, but when the pH is higher the inactivation becomes more pronounced, until the enzyme at pH = 12 is destroyed almost immediately. The swelling of the undissolved albumin is of importance for its solution, but the reaction of the maximum swelling is at the point where the trypsin is immediately destroyed, namely at pH = 12.3. The destructive action of the trypsin on fibrin is dependent upon the H-ion concentration.

(1b—19)

**The Proteins of the Alfalfa Plant.**

*Thomas B. Osborne, Alfred J. Wakeman and Charles S. Leavenworth, J. Biol. Chem., 49:63, Nov., 1921.*

It was found possible to grind the fresh green alfalfa plant so thoroughly that practically all of the contents of its cells could subsequently be extracted by water, alcohol, dilute aqueous alkali and hot alkaline alcohol, applied in the order named. Water was found to extract over 45% of the dry matter of the plant, nearly 43% of the ash-free solids, nearly 44% of its nitrogen and almost 71% of its inorganic constituents. By subjecting the ground plants to high pressure, relatively large quantities of the undiluted juice of the plant could be obtained as an almost clear dark brown liquid free from chlorophyl, or other suspended particles. This juice contains about 10% of solids partly in colloidal solution. The addition of about 20% alcohol causes the latter to fall as a flocculent precipitate which can be filtered out. The filtered solution contains considerable nitrogen but less than 1% protein. Some of this protein can be coagulated by heating the acidified solution, but more of it has properties characteristic of proteoses. Most of the protein in the aqueous extract is in the precipitate produced by alcohol, which contains the substances previously in colloidal solution. In addition to protein, which forms upwards of 70% of this precipitate, there are also present calcium phosphate and calcium salts of organic substances which can be extracted from the protein by alcohol containing HCl in which the protein is insoluble. The organic substances appear to be largely pigments which resemble the flavone derivatives already known to occur in many species of plants.

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**The Catalytic Effect of Ammonia on the Oxidation of Butyric Acid with Hydrogen Peroxid.**

*Edgar J. Witzemann, J. Biol. Chem., 49:123, Nov., 1921*

These experiments were undertaken to determine the reason for the difference in results obtained in the oxidation of butyric acid with hydrogen peroxid in the presence of different alkaline substances. In the presence of potassium hydroxid in amounts varying from 0.20 to 4.0 equivalents it was found that no appreciable oxidation of butyric acid took place, as was proved by the almost quantitative recovery of the unchanged acid, but in the presence of ammonium hydroxid in amounts varying from 0.20 to 10.0 equivalents much oxidation took place. It was found that the amount of oxidation in the presence of ammonia increased with increase in the ammonium hydroxid, other things being equal, until more than 4.0 equivalents of ammonium hydroxid were present; after which it decreased somewhat. This decrease with large excess of ammonium hydroxid was due to the spontaneous liberation of oxygen by the action of ammonium hydroxid on the hydrogen peroxid, before it could be utilized in oxidation. If 1 equivalent of both ammonium hydroxid and potassium hydroxid be used, more oxidation takes place than if 2 equivalents of either of these bases are added. Witzemann remarks that the type of oxidation observed in these experiments was mainly of the beta type or the conversion of butyric acid into acetone and 1 molecule of carbon dioxid. He suggests that the ammonia effect described may be the agency by which the normal oxidation of

(1b—19)

fatty acids is brought about in the liver, because in the liver the substances required for this effect are all available and furthermore this organ normally shows the greatest tendency to form aceto-acetic acid.

(1b-21)

**The Analysis and Differentiation of Acetaldehyde, Aldol and Glyoxylic Acid, and Their Appearance in Diabetic Urine.**

*Robert Fricke, Hoppe-Seyler's Ztschr. f. Physiol. Chem., 116:129, Berlin, Sept. 26, 1921.*

The acetaldehyd demonstrated by Stepp and Feulgen in the urine of diabetics indicated a probable connection between the aldol sometimes found in large quantities and the acetone bodies in the urine. Ten c.c. of a 10% solution of aldol with 4 gm. dimedon dissolved in alcohol, after having been left standing for half a day and with the addition of NaCl precipitated crystalline aldolmedon with a melting point of 172° C.; this was recrystallized in 50% alcohol. The aldolmedon when it had been recrystallized in 96% alcohol changed into crotonmedon, melting point 183°. Both showed slight solubility in most of the organic solvents except ligroin and carbon bisulphid. Condensation products of acetaldehyd, melting point 148°, prepared with dimedon and easily soluble in ligroin, furfrol, glyoxylic acid, and formaldehyd, were tested;  $\beta$ -oxybutyric acid, crotonic acid, acetic acid, uric acid, acetone, glycosin and formic acid among the substances existing in the urine were found not to react with dimedon. On the basis of these results, there was found in 15 liters of acid diabetic urine, minimum quantities of a body which volatilized with steam and which reacted markedly with dimedon, reduced an ammoniacal silver solution, and was of the nature of the aldehydes. Acetaldehyds and furfrol resulting from glyoxylic acid must be excluded, but crotonaldehyd resulting from aldol probably exists. In 3 cases of diabetes which were examined, the presence of aldol could be disproved, but the acetaldehyd first demonstrated by Stepp and Feulgen was clearly demonstrated.

(1b-22)

**Albuminoids of Basic Nature.**

*K. Felix, Hoppe-Seyler's Ztschr. f. Physiol. Chem., 116:150, Berlin, Sept. 26, 1921.*

An albumin derivative of basic nature was produced from the intestinal membrane, from the lymphatic glands and from the thymus gland by removing the fatty and connective tissues, mincing, extraction with alcohol and ether, and extraction with diluted hydrochloric acid. The extract was filtered and neutralized, the histon precipitated with NaCl, and the NaCl removed by repeated evaporation and dilution. The biuret reaction of the filtrate was positive; the diazo reaction negative. The filtrate was concentrated,  $H_2SO_4$  added and precipitated with phosphotungstic acid. The phosphorous tungstate was decomposed by baryta the latter removed by  $CO_2$  and the syrup resulting after evaporation treated with alcohol, after which the sulphate separated out in floccules. The yield was slight. The substance was free from phosphorus and as no increase of free amino groups was found by the Van Slyke micro-apparatus, it was not treated with trypsin. The nitrogen determinations were made by the method of Kossel and Kutscher.

The basic albuminoids differ in chemical composition and their physiologic significance has not been determined. The substances have not been named, but that derived from the thymus gland is perhaps thymamin.

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(1b-23)

**Modern Investigations on the Breaking Down of Urea by the Enzyme Urease.**

*Emil A. Werner, Dublin J. M. Sc., 4:512, Nov., 1921.*

The "alkaline fermentation" which urine quickly undergoes when exposed to the air has been considered, up to the present time, as a simple process of hydrolysis according to the equation suggested by Dumas in 1830. All investigators (many of whose results are here reviewed) have left unanswered the question, "What is the mechanism by which urease brings about the destruction of urea at a comparatively low temperature?" It was proved by the author (1918) that urea in solution in the presence of either acids or alkalis is not hydrolyzed at the ordinary temperature, and any change in this direction, which must be preceded by dissociation of urea, is perceptible only at about 60°, and is even then extremely slow. In fact, according to Werner's explanation, urea is not hydrolyzed at all; it is dissociated by heat into ammonia and cyanic acid, HNCO, and the latter is then hydrolyzed with the equation suggested by Dumas as the final result. There is no doubt that urease attacks "free" urea only, and it has been proved by the writer that dissociation into ammonia and cyanic acid is the first step in all the decompositions of urea in this condition. Can urease initiate this dissociation as the first step in the "hydrolysis" of urea? A comprehensive study of the urea/urease system, recently carried out by Fearon on the basis of the cyclic formula of urea, is here summarized as giving an affirmative answer to this question. Fearon's explanation of the mechanism of reaction is: Urease condenses urea by adsorption on its surface. This is followed by the dissociation of the urea into ammonia, which combines with the enzyme, and cyanic acid which is hydrolyzed by the solvent. Dissociation of urea may be brought about by pressure in the adsorption area, temperature of adsorption, effect of an electric surface field—since urease has been found to carry an electro-negative charge and to combine with ammonia. The function of the enzyme (urease) is to bring about dissociation of urea into ammonia and cyanic acid. The hydrolysis of the latter follows as a secondary change in the presence of water. Urease is not directly concerned in the "hydrolysis."

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(1b-24)

**The Determination of Purin Bases in the Urine.**

*H. Steudel and Sung-Sheng Chou, Hoppe-Seyler's Ztschr. f. physiol. Chem., 116:223, Berlin, Sept. 26, 1921.*

In following the Krüger method (calcium sulphate with sodium bisulphite) of determining the purin bases in the urine, it was observed, while concentrating the filtrate after the second copper precipitate with a weak hydrochloric acid reaction, that the white crystals of the chlorids of the purin bases were abundantly mixed with crystals of ammonium chlorid. The nitrogen in this fraction having been determined by Kjeldahl's method and its value compared to the purin bases in the liquid, it was found that the determination of the contents of purin bases was

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too high, namely 0.011 instead of 0.016. The origin of this NH<sub>3</sub> was not determined. In order to remove this source of error it is proposed, that after decomposing with H<sub>2</sub>S the filtrate of the second copper precipitate be boiled in an excess of mangnesium oxid until the NH<sub>3</sub> has been removed.

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**Observations on the "Alkaline Tide" After Meals. I.**

*Cyrus H. Fiske, J. Biol. Chem., 49:163, Nov., 1921.*

The observations reported in this paper (the nature of the variations that may occur in the CH of urine from hour to hour) were taken from experiments, all on the same subject, made primarily for other purposes. The hydrogen-ion concentration was determined colorimetrically by a modification of the dilution method as follows: In each instance, 1% of a one hour sample of urine (or its equivalent) was diluted to 10 c.c. and compared with a fresh standard (made by adding carbonate-free standard alkali to acetic acid, monopotassium phosphate, or borate-KCl mixture, and diluting to a concentration of 0.01 M). The indicators used were methyl red, brom-cresol purple, phenol red, and cresol red. This form of the colorimetric method measures the CH of the urine, not as secreted, but after dilution to a uniform basis. The acidity was determined by titrating with standard alkali from a microburette to match a standard 0.01 M phosphate mixture (pH 7.4), prepared as described above. The indicator was phenol red and no oxalate was used. The possibility of error from the effect of calcium was further eliminated by repeating each titration in the presence of twice as much water. The author's tabulated results show that the urine usually becomes quite suddenly less acid (and sometimes alkaline) in the second or third hour after a meal. When the meal is a full one the CH at that time is ordinarily much lower than it is likely to be otherwise. But when the meal is small it is usually impossible to decide whether the "tide" is due directly to the meal under consideration or to a delayed effect of a previous meal, or whether it is in fact anything more than an apparent alkaline tide, representing in reality the recovery from a temporary increase in acidity immediately following the meal. In the author's opinion whether or not it may be correct to say that the alkaline tide is due to the secretion of hydrochloric acid by the stomach, it is certain that the acidity of urine after meals is influenced by various factors operating at the same time. The maximum alkalinity after a protein meal is often reached at a time when the excretion of sulphate and phosphate has reached or is approaching a maximum, and any decrease in acidity occurring then must be in the face of this additional acid production. The author also believes it is safe to suppose that the intensity of the tide, or its appearance at all, will depend not only upon the amount of hydrochloric acid secreted by the stomach, if that is one of the factors involved, but also in an independent way upon the composition of the food.

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**Inorganic Phosphate and Acid Excretion in the Postabsorptive Period.**

*Cyrus H. Fiske, J. Biol. Chem., 49:171, Nov., 1921.*

In a study of one hour urines collected during the morning of the first day of fasting, the author was struck by the apparently unaccountable (Sec. 1—Page 63)

able increase in the phosphate output, which reached its maximum about the middle of the afternoon. Further inquiry immediately showed that this rise begins soon after the drop long known to occur during the night has reached its lowest point, which may be as low as 6.3 mg. of phosphorus per hour under these conditions. A curve of this same general form was found by the author in about 40 such experiments on 4 subjects, but he has confined this paper to experiments selected from about 25 performed on the fourth subject. The experiments involved determinations, not only of phosphate, but also of several other factors concerned in the question of acid excretion (which likewise is subject to variations of considerable magnitude during the postabsorptive period). The object was to attempt to learn the reasons for these changes as a whole. No vigorous exercise was permitted during the course of any of these experiments. The subject was on an ordinary mixed diet divided into the customary 3 meals a day with no attempt to maintain constancy of composition.

The tabulated results showed oscillations in the curve of phosphate excretion which bore no relation to the volume of urine, but suggested some relation to the alkaline tide observed by Hasselbach during the morning in subjects who had been without food since the previous noon. In order to intensify the alkaline tide the subject was given 200 c.c. of milk at midnight. The temporary drop in the CH of the urine during the following morning was then ordinarily much more pronounced, and the more so the larger amount of milk taken. The author remarks the variations observed in the excretion of inorganic sulphate can furnish no basis for explaining the alkaline tide by alterations in the rate of sulphuric acid production, since the tendency throughout is for the inorganic sulphate content of the urine to decrease gradually to an approximately constant level, with no significant rise in the latter part of the day. The author believes his observations as a whole, in so far as they can be accounted for at all by those factors that have been determined in these experiments, can be interpreted only upon the basis of a decrease (followed by a rise) in the rate of production of phosphoric acid during the morning; or, what is perhaps more probable, an active re-tention of phosphate (phosphoric acid or primary phosphate) which, later in the day, is released.

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**Studies in the Physiology of Vitamins. I. Vitamin-B and the Secretory Function of Glands.**

*George R. Cowgill and Lafayette B. Mendel, Am. J. Physiol., 58:131, Nov. 1, 1921.*

The experiments herein described were undertaken to test experimentally the hypothesis that vitamin-B functions as a chemical entity which stimulates glands to secretory activity. Preparations containing vitamin-B were made from wheat embryo, yeast, rice polishings and navy bean. The preparations were shown to contain vitamin-B by tests upon polyneuritic dogs and pigeons. These solutions were then tested for their possible action on the secretory function of the pancreas, liver and salivary glands. The effect of the products on the rate of flow of pancreatic juice and bile was noted in anesthetized dogs, in which the pylorus was ligated to prevent secretion due to discharge of acid chyme from the stomach, and the discharge of gall-bladder bile was prevented

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by ligation of the cystic duct. Fresh secretin solutions were injected for comparison. Each product was also tested for its possible action on the secretory function of salivary glands of anesthetized dogs in which the ducts from the submaxillary and sublingual glands were cannulized. In such procedures stimulation of the chorda tympani nerve and the injection of pilocarpin served as control procedures. The effect of the products on secretory glands was noted in dogs which had subsisted on a normal mixed diet and in dogs which had been fed a diet free from vitamin-B. The tabulated results show that there is no direct relation between vitamin-B and the secretory function of the pancreas, liver and salivary glands.

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**The Rôle of Microörganisms in the Production of Vitamins.**

*E. Wollman, Compt. rend. Soc. de biol., 85:801, Paris, Nov. 5, 1921.*

Two series of tests were made in guinea-pigs and pigeons. Production of the antiscorbutic vitamin by *Bacillus bulgaricus* was attempted in the first series, production of the anti-neuritic (anti-beriberi) vitamin in the second, by amylo-mucor. Neither microörganism produced a vitamin. The second series of tests contrasts amylo-mucor with yeasts, which contain the anti-neuritic vitamin.

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**Vitamin Content of Rice by the Yeast Method. Organic Nitrogen as a Possible Factor in Stimulation of Yeast.**

*William D. Fleming, J. Biol. Chem., 49:119, Nov., 1921.*

The author estimated the water-soluble B content of a particular lot of rice by the yeast cell method. The technic of Fulmer, Nelson, and Sherwood was used for estimating the growth of the yeast. An extract of Fleischmann's yeast in 0.1% acetic acid was used as a standard source of water-soluble B. For purposes of comparison, extracts in 0.1% acetic acid of samples of rice of the same growing but in varying stages of milling and polishing were used. The rice under investigation was likewise used in extract in 0.1% acetic acid. The results of the cultures after additions of these extracts were similar to the results of similar experiments by previous workers. In general the growth of the yeast was proportional to the amount of extract added; the growth was not only greater with increasing amounts of extract but, in the case of yeast and of rice supposedly rich in water-soluble B—unhusked and brown rice—the rate of increase in growth per unit weight of extract added, was greater. However, when these stimulating extracts were so treated with alkali as to destroy any water-soluble B they might contain, results were obtained which the author believes disproved a specific action of water-soluble B in stimulation of yeast growth.

The author found that the addition of organic nitrogen to the inorganic nitrogen of the culture medium is one factor in the stimulation of yeast growth.

**1c. PHARMACOLOGY AND TOXICOLOGY**

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**Pharmacologic Studies on Normal and Diseased Subjects.**

*A. Bornstein, Deutsch. med. Wochenschr., 47:1200, Berlin, Oct. 6, 1921.*

This study deals with the effect of atropin in diabetes. Adrenalin, by stimulation of the sympathetic system, may cause the liver to transform glycogen into sugar and thus produce glycemia. Pilocarpin, physostigmin, cholin and acetylcholin stimulate; while atropin paralyzes the parasympathetic system. According to Langley the parasympathetic system is a part of the vegetative nervous system which does not belong to the sympathetic system. Moderate doses of pilocarpin produce glycemia which may be prevented by the preliminary administration of atropin. Pilocarpin glycemia is less intense than sympathetic glycemia and therefore only exceptionally causes the excretion of sugar in the urine. The sugar is oxidized very quickly in the blood so that the glycemia, unlike that due to adrenalin, does not reach very high values. These results were found in animals. A study of the effect of atropin on blood sugar was also made on diabetic patients. Diabetics at first show less general reaction to atropin than normal men. An increase of 20 or 30 pulse beats which takes place in normal cases only occurred after the giving of 2-3 mg. to diabetics. In 9 of 12 cases of diabetes the sugar in the blood decreased, which could only have been caused by the atropin. It seems that cases with a higher blood-sugar content react more readily to atropin than those with low sugar content. Atropin may be valuable as a supplement to dietetic treatment in cases where it is important to get rid of sugar quickly, or in cases where the withdrawal of carbohydrates would involve too great a danger of acidosis.

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**The Influence of the Electric Current on the Absorption of Drugs.**

*O. Inchley, J. Pharmacol. & Exper. Ther., 18:241, Nov., 1921.*

To determine within what limits the electric current facilitated absorption from the skin, experiments were performed principally on living animals, cats, guinea-pigs and rabbits. The animals were anesthetized with urethane by means of which constant blood-pressure and respiration can be obtained for some hours. In some cases the skin to which the electrode was applied for the purpose of conveying in the drug was prepared a day or two previously, either by shaving the part free from hair, or by destroying the hair with barium sulphid. In other cases the hair was left intact. No appreciable difference was noted. The current (amperage) and the area of the skin to which it was applied were noted, and the current was kept constant throughout the experiment. The voltage was gradually raised or lowered when required, and as far as possible all sudden alterations were avoided. Blood-pressure when necessary was taken from the carotid artery, respiration was recorded from a tambour placed on the sternum. Coagulation time was obtained when required by drawing a drop of blood from the ear and estimating by a method described. A number of experiments have also been performed on dead tissues, and on various isolated organs. It was found that both positive and negative ions can be absorbed through the

skin or mucous membrane by means of the electric current if solutions of the drugs are applied at the appropriate electrode. The current is conveyed through the body by the tissue ions. After the introduction into the body of the foreign ion, the current has no further appreciable influence on it. With a current localized in the tongue, the atropin ion rapidly reaches the heart. The ferricyanid ion penetrates through the skin, but after this the electric current has no further influence.

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**On the Influence of Colloids on the Action of Non-Colloidal Drugs. III.**

*W. Storm van Leeuwen and A. von Szent-Györgyi, J. Pharmacol. & Exper. Ther., 18:257, Nov., 1921.*

In former publications it was pointed out that the inhibitory influence of colloids on drugs possesses two interesting features: (1) The inhibitory action of colloids is very specific; (2) the inhibition is brought forth not by a chemical destruction of the drug, but by an adsorption of the drug, or at least by a physicochemical process, closely related to adsorption. Colloids cannot only inhibit the action of alkaloids, but may also increase this action. An attempt has been made to identify the substances in rabbit serum which are responsible for the described effect, after a preliminary study of some of the lipoids which are known to occur in serum. In the first experiments lecithin and cholesterin were found to increase the action of pilocarpin on the isolated gut, but the action was not constant. The action of lecithin was investigated in 13 experiments. In 6 cases the lecithin was inactive, in 5 cases it had a distinctly promoting effect on the action of pilocarpin, and in 1 case the action of pilocarpin seemed to be weakened a little by lecithin. The next lipoid to be investigated was cholesterin. Here also a distinct effect was found, but here also the phenomenon was not always demonstrable. Cerebron and cephalin were also studied. Cerebron had a distinct though slight effect on the pilocarpin action. The action of cephalin was much more pronounced, but here the same difficulty was met as in the case of lecithin: the action was not constant. Protargol showed a distinct promoting influence in 3 cases, but was inactive in other instances. Nucleic acid was also slightly active sometimes, but not constantly. Starch, bolus alba, gelatine, agar, kaolin, stearic acid, salts, casein, hemoglobin, egg-white were all negative. Pepton had, in a number of experiments, a very distinct promoting effect on the pilocarpin action.

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**On the Influence of Colloids on the Action of Non-Colloidal Drugs. IV.**

*W. Storm van Leeuwen and A. von Szent-Györgyi, J. Pharmacol. & Exper. Ther., 18:271, Nov., 1921.*

Research was started with the purpose of finding an explanation for the differences in the binding power of serums of various animals; the problem has not been cleared up entirely. Even if every influence that can be controlled is kept constant, very large differences between different animals are found. The absorption of pilocarpin by rabbit serum can be inhibited by chloroform and still more strongly by ether, in concentrations which occur in the blood during narcosis. Peptone has a similar effect, but urethanel, magnesium sulphate, starch and lecithin

have no influence in this respect. It was pointed out previously that the formation of anaphylatoxin in vitro, by addition of agar, gelatin, etc., to guinea-pig serum, may depend on changes in the relation between the various colloids in the serum, through which change the action of poisons already present in the serum may be intensified. The experiments reported in the present paper suggest another possibility. If an innocuous serum (rabbit serum plus pilocarpin, or rabbit serum plus atropin) can become highly poisonous by the mere addition of peptone (which loosens the binding of pilocarpin and atropin to serum substances), it is conceivable that similar phenomena occur when innocuous guinea-pig serum becomes poisonous by the addition of agar, gelatin or inulin. It is beyond doubt that under physiologic conditions various poisons occur in animal blood. It is highly probable that the action of these poisons will be influenced by the various colloidal substances present in the serum. This influence may be inhibitory or augmentor. If by the mere addition of a small quantity of ether to a mixture of serum plus pilocarpin the action of this mixture on the isolated intestine can be increased many times, by the inhibiting action of the ether on the pilocarpin absorption, it is probable that similar processes may occur in the animal body during narcosis.

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**Systematic Effects of the Intravenous Injection of Solutions of Various Concentrations with Especial Reference to the Cerebro-spinal Fluid.**

*Lewis H. Weed and Walter Hughson, Am. J. Physiol., 58:53, Nov. 1, 1921.*

The authors state the purpose of this paper is to record the general systemic effects of the intravenous injection of solutions of various concentrations. For the experiments, etherized cats were used. The arterial, venous and cerebrospinal fluid pressures and the urinary output were determined first. Then the injections of foreign solutions were given from a buret connected to a cannula introduced into a vein, usually the superficial brachial. Control observations were made on etherized animals, the procedures being limited to the operative measures incidental to the attachment of the various manometers. The foreign solutions employed were: (1) Ringer's solution; (2) distilled water (hypotonic solution); (3) a 30% solution of NaCl in water, or (4) "concentrated Ringer's solution." The authors' results are plotted and the graphs show that the intravenous injection of relatively large amounts of Ringer's solution causes a temporary rise in the pressure of the cerebro-spinal fluid and in the brachial venous pressure; both quickly return to normal levels. Arterial pressure is usually reduced during the period of injection. The intravenous injection of a hypotonic solution (distilled water) causes a prolonged increase in the pressure of the cerebro-spinal fluid. This increase in pressure is accompanied by an increase in brachial venous pressure of smaller degree and of shorter duration. Arterial pressure rises slightly. The intravenous injection of strongly hypertonic solutions causes a prolonged and profound fall in the pressure of the cerebrospinal fluid preceded usually by a sharp rise. Venous pressure is increased and arterial pressure lowered during the injection period. The authors remark that cerebrospinal fluid pressure is invariably higher than that of the brachial vein except after the intra-

venous injection of strongly hypertonic solutions. The changes in cerebrospinal fluid pressure induced by these injections appear to be independent of the changes in the systemic arterial or venous pressures.

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**Intracranial Venous Pressure and Cerebrospinal Fluid Pressure as Affected by the Intravenous Injection of Solutions of Various Concentrations.**

*Lewis H. Weed and Walter Hughson, Am. J. Physiol., 58:101, Nov. 1, 1921.*

The effects are detailed of the intravenous injection of solutions of various concentration upon the cerebrospinal fluid, the sagittal and brachial venous pressures, the carotid systolic pressure and the urinary output. The technic employed is the same as that previously described by the authors. The sagittal venous pressure was obtained as follows: The superior sagittal sinus was exposed over the posterior one-third of its course by carefully removing the bone in a small sagittal groove by means of a rongeur. This exposure was quickly made without injury to the dural walls of the sinus and in the usual experiment the dark channel of the venous sinus was seen coursing in the bony opening. The pressure of the cerebrospinal fluid was then taken and the readings of the normal level were obtained. With the manometer for the fluid pressure in place, a shortened lumbar puncture needle was inserted posteriorly in the superior sagittal sinus to the torcular herophili. The needle after insertion was firmly held in place and the bony groove filled with bone wax to prevent bleeding. With the withdrawal of the stylet from the needle, blood came freely from the open end; connection was then quickly made to a calibrated manometer of 1 mm. bore, filled with a 4% solution of sodium citrate. By means of a three-way stop cock the needle was kept free of blood clots, frequent washings being necessary to accomplish this. Pulsations of from 2 to 4 mm. excursion were observed throughout the experiment. The values of the 4% citrate solution was transposed into terms of Ringer's solution so as to be directly comparable to the pressures of the cerebrospinal fluid and of the brachial vein. Control observations were made in which the manipulative procedures were limited to those required for the attachment of the recording instruments.

The results obtained following the intravenous injection of (a) concentrated Ringer's solution, (b) distilled water (hypotonic solution) or (c) 30% solution of NaCl (hypertonic solution), have been plotted graphically. They show that under the conditions of experimentation, the pressure of the cerebrospinal fluid remains constant with only minimal fluctuation; brachial and sagittal venous pressures likewise show no marked or abrupt changes in tension. But with the intravenous injection of Ringer's solution in large amounts, the short-enduring rise in the pressure of the cerebrospinal fluid is accompanied by a smaller rise in the sagittal venous pressure and by an even smaller increase in the brachial venous pressure. After the intravenous injection of a hypotonic solution (distilled water) the greatest rise occurs in the pressure of the cerebrospinal fluid, a lesser but still considerable increase in the sagittal venous pressure and a still smaller augmentation of the brachial venous pressure. Two phases occur in the reactions of these pressures to the intravenous injection of strongly hypertonic solutions: in the

first, during the period of injection, increases are found in the brachial and especially the sagittal venous pressures. After an initial fall the cerebrospinal fluid pressure usually rises. Later all three pressures fall, especially that of the cerebrospinal fluid. Brachial and sagittal venous pressures are reduced, especially the latter which may reach a level from zero to 40 mm. above zero.

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**The Chemotherapy of Antimony. Comparison of the Antimonyl Tartrates with the Organic Compounds of Antimony.**

*Robert George Fargher and William Herbert Gray, J. Pharmacol. & Exper. Ther., 18:341, Dec., 1921.*

During the last decade antimony has assumed a new importance from the use of tartar emetic in certain tropical diseases of parasitic origin. Results of sufficient importance have been obtained in the treatment of trypanosomiasis, bilharziasis, and leishmaniasis to necessitate search for more favorable means of administering antimony. Prior to this study, experiments had been in progress with the object of studying (a) the effect of variation of the basic radicle in the emetics, (b) the replacement of tartaric acid by other suitable acids, and (c) the question of the relative merits of the true organic compounds of antimony and the emetics. Representative specimens of these three types have been prepared and their toxicity determined by intravenous injection in mice. The toxicologic work has been undertaken by Trevan, who proposes to examine the precise pharmacologic action of the drugs. Trials of all members of this series on diseases experimentally induced in rats and other animals are also in progress. The salts examined comprised those of the alkali metals (potassium, ammonium, sodium and lithium); the cinchona alkaloids (quinin, quinidin, hydroquinin, cinchonin, cinchonidin and quinotoxin); anilin and p-phenetidin; ethylenediamin and butylamin and glyoxalin. The general conclusion may be drawn that a variation of the base in the antimonyl tartrates considerably decreases the toxicity per unit of antimony, the most favorable salts being those of quinin and p-phenetidin. Aqueous solutions of quinin and quinidin tartrates behave differently on boiling with antimony trioxid, the quinin being transformed almost completely into the more toxic quinotoxin, while the stereoisomerid quinidin is unaffected. The results so far obtained in the replacement of tartaric acid by other acids, show little of pharmacologic interest. In regard to the organic compounds of antimony, in no case have the salts been obtained in a crystalline condition, and the same is true of numerous parallel attempts with the potassium and lithium salts. Sodium m-acetylaminophenylstibinate is the least toxic. The others are much less favorable.

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**Experimental Researches on a New Organic Arsenical Preparation, Which Can be Injected Intramuscularly.**

*E. Jeanselme and M. Pomaret, Bull. Acad. de méd., 86:219, Paris, Nov. 1, 1921.*

In preparations of the type of neosalvarsan the addition of side chains to the salvarsan nucleus has certain advantages in solubility or stability but none in therapeutic effect, for their reducing properties retard the transformation of the nucleus into spirocheticidal substances.

Attention has been called to the fact that the phenomena of shock which are produced by these preparations are due to intravascular flocculation caused by the carbolic acid radicles, which is the more likely to occur as the alkaline reserve of the blood is low. Maximum therapeutic results, without the production of shock, may be obtained with intramuscular injections.

The authors have therefore sought a product which would be alkaline and could be administered intramuscularly without causing pain or local reactions. Ehrlich's "592" is such a preparation, but it could not be used without modification on account of its insolubility and easy transformation into toxic products. By making it stable in an organic alkaline medium it does not possess the flocculating properties of ordinary arsenical preparations. This new product (132) is only slightly toxic in spite of the fact that it contains 40% of arsenic. A dose of 0.15-0.16 gm. per kilogram is tolerated by the rabbit, corresponding to about 0.30 gm. of neosalvarsan.

Intravenous injection of 0.40-0.50 gm. in dogs weighing 10-12 kgm. produced no cardiovascular action. In experimental syphilis of rabbits, 0.0037 gm. per kilogram was sufficient to cure a chancre, that is, only one-fortieth of the toxic dose.

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**Effects of Arsenic on Development of the Bones.**

*A. Van den Eekhout, Compt. rend. Soc. de biol., 85:740, Paris, Oct. 22, 1921.*

Experiments were made on rabbits, small doses of arsenic being employed (1 mgm. daily for from ten to thirty days, then 2 mgm. daily for ten days). The factors checked were the weight, length and structure of the femur and tibia, and the weight of the animal. Bone weight was determined after drying, the fat being removed with ether. Small doses of arsenic administered to healthy, well nourished rabbits has little influence on the general state of nutrition, bodily development or length. Bones are rendered denser, heavier and more resistant.

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**Anticoagulant Action of the Arsenobenzenes. Effects on Globulins.**

*C. Flandin and A. Tzanck, Compt. rend. Soc. de biol., 85:852, Paris, Nov. 12, 1921.*

Blood is collected in a glass tube, the walls of which have been moistened with a 10% solution of an arsenobenzene (novarsenobenzol, sulpharsenol), and shaken to bring it into contact with the reagent, which renders the blood incoagulable. Sedimentation yields a layer of red-cells, at the bottom of the tube; a milky ring made up of leukocytes and globulins; and, above, a zone of clear plasma. The authors wished to determine whether the globulins were agglutinated, as in blood rendered incoagulable by peptone, or free, as in blood made incoagulable by sodium citrate. The globulins were not agglutinated, and the arsenobenzenes behaved in the same manner as sodium citrate.

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**Physiologic Researches on Shock and Arterial Hypotension Caused by Arsenobenzol Preparations, and Hypertension Produced by Arsenoxid.**

*Pomaret, Bull. Soc. fran<sup>c</sup>. de dermat. et de syph., Paris, No. 8, 1921, p. 415.*

From an analysis of the physical and chemical reactions taking place in vitro between the albuminous elements of blood serum and arsenic or novarsenobenzol preparations, it can be stated that in very weak acid media a complex protein and arsenophenolic adsorption compound is precipitated. The formation of this compound depends directly on the phenol radicals contained in the arsenical preparations, and as a matter of fact the injection of trinitrophenol in dogs produces exactly the same effects on the blood pressure as 606, when the latter is not neutralized with sodium hydroxid. The rôle of the phenol radical in the arsenobenzol molecule being thus definitely established, experiments were made with arsenoxid, one of the occasional elements of arsenobenzol preparations. When injected intravenously in the form of aqueous solutions of the hydrochlorate of aminophenol arsenoxid, it produces in animals considerable hypertension, slowing of the heart beat and marked increase of the amplitude of the contractions. This substance is not therefore responsible for the hypotension which sometimes follows the injection of arsenobenzol; this experiment confirms the importance of the rôle of the phenol radical in the production of shock.

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**A Study of Antispasmodic Drugs on the Bronchus.**

*David I. Macht and Giu-Ching Ting, J. Pharmacol. & Exper. Ther., 18:373, Dec., 1921.*

A number of drugs were studied with respect to their action on the bronchi by the "direct method," that is, on excised surviving bronchial preparations of the pig. Relaxation of bronchial muscle may be produced by drugs either through a direct action on the muscle cells themselves or on the sympathetic, parasympathetic or ganglionic terminal structures of the bronchi. The most powerful bronchodilators were (1) papaverin and various benzyl compounds, which act on the muscle cells, (2) atropin, which exerts its action through paralysis of the parasympathetic myoneural junctions, and (3) epinephrin, which produces active stimulation of the true sympathetic dilator terminals. The iodid, bromid, and nitrite ions produced a relaxation of the bronchial muscle. This effect, however, is probably considerably minimized in the intact body. A chemicopharmacodynamic relationship of practical interest has been traced in connection with the action of various xanthin derivatives on the bronchial muscle. The intensity of the action of various antispasmodic drugs on bronchial muscle varies to some extent with the previous tonicity or spasticity of the bronchus. A distinct difference in reaction to drugs has been found between the fresh surviving bronchi from healthy lungs and from lungs with more or less pathologic change.

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**Experimental Inquiry into the Sedative Properties of Some Aromatic Drugs and Fumes.**

*David I. Macht and Guo-Ching Ting, J. Pharmacol. & Exper. Ther., 18:361, Dec., 1921.*

The effects of a number of odoriferous substances were determined by the behavior of rats in the circular maze. It was found that valerian and asafetida exert a distinctly sedative effect, whereas the inhalation of fumes of various samples of incense did not produce any depressant effect unless the fumes were so heavy as to render intoxication with poisonous gases probable.

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**The Physiological Standardization of Extract of Belladonna.**

*W. Storm van Leeuwen and P. H. Maal, J. Pharmacol. & Exper. Ther., 18:313, Nov., 1921.*

Samples of belladonna-extract were procured from 6 different apothecaries and the strengths determined by physiologic methods. Portions of the samples were sent to Meulenhof of Zwolle, who made chemical determinations following exactly the prescriptions of the Dutch pharmacopoeia. Two dogs were used, each of which had a permanent fistula of one of the submaxillary ducts, and Cushry's method applied. After determination of the amount of atropin which in each dog was necessary to inhibit the increased secretion of saliva produced by the injection of pilocarpin, various quantities of each sample of extract of belladonna were injected until it was found that a quantity ( $x$ ) of the belladonna solution was weaker than ( $y$ ) of atropin, while  $x + a$  of hyoscyamin was stronger than  $y$  of atropin. As recent work has shown that wild belladonna, and even the cultivated plant and the extract, contain almost exclusively hyoscyamin (only very small quantities of atropin being found), and as the action of hyoscyamin on the salivary gland is twice as powerful as the action of atropin, the values were divided by 2 in order to be comparable with the results of the chemical determinations. The values are tabulated. In some instances the results of the physiologic and chemical determinations agreed fairly well. In 2 instances there were remarkable differences, and in 1 sample there was no agreement at all. This last result is explained in 1 of 2 ways: Either the extract of belladonna contained, in that instance (besides a certain amount of hyoscyamin) a quantity of an alkaloid which has a more powerful action on salivary secretion than hyoscyamin; or belladonna contains substances which increase the action (or promote the resorption after subcutaneous injection) of hyoscyamin. The first assumption is considered improbable, since no alkaloids of a stronger action on salivation than hyoscyamin are known. In all cases where accurate prescriptions are wanted, a standardized preparation should be used; "standardized extract of belladonna" is considered a preparation containing exactly 1.15% of alkaloids for Holland or 1.18-1.32% for the United States (determined by means of the usual chemical method), which gives (when standardized physiologically) a value not differing materially from 1.15% (1.18 to 1.32%) of hyoscyamin.

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**Some Differences in Response to Atropin in White and Colored Races.**

*H. A. Paskind, J. Lab. & Clin. Med., 7:104, Nov., 1921.*

Normal subjects, twenty white and twenty negro patients, were used to compare the action of small doses on the two races. McGuigan had found that small doses always caused a slowing of the pulse, but the experiments made by the writer show that this holds true only exceptionally with negroes. In them there is not the initial showing, which is marked in white subjects. In 3 typical protocols of tests on black men, the heart rate remained unchanged for a period varying from ten to twenty minutes, after which acceleration began. In 3 similar tests on white men an initial slowing, lasting about twenty minutes, occurred in all, after which the heart rate increased beyond the normal. The acceleration was about the same in both white and black subjects. With larger doses the slowing is very transient in whites but may elicit a slowing in the negro pulse. These facts demonstrate a relative insusceptibility of the negro.

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**Further Observations on the Pharmacology of Benzyl Compounds.**

*Carl Nielsen and John A. Higgins, J. Lab. & Clin. Med., 7:69, Nov., 1921.*

The authors have already published results showing that benzyl benzoate and benzyl cinnamate produce relaxation in situ of the longitudinal muscles in the dog and cat. The findings in the present paper were nearly all obtained with the Trendelenburg method and include experiments on blood-pressure, respiration and intestinal movements.

Twelve benzyl compounds were investigated. All of these produced a fall in blood-pressure when injected intravenously. Respiration was also depressed by relatively large doses, sometimes actually stopping while the heart was still beating. All of the compounds produced relaxation of intestinal muscle. The power of producing relaxation in smooth muscles was, in the simple benzyl esters, proportional to the rate of hydrolysis, but this was not the case with the benzyl esters containing substituting groups, such as benzyl salicylate and benzyl acetylsalicylate. With these the power to relieve pain is not a simple function of the rate of hydrolysis to benzyl alcohol.

Of the twelve compounds benzyl acetylsalicylate relaxed intestinal muscle most, benzyl salicylate next. In order to investigate the entire series under comparable circumstances a solvent (sweet almond oil) had to be chosen that was suitable for the esters that are solid above body temperature. The oily solutions (1:5), injected at a little above body temperature ( $39^{\circ}$ - $40^{\circ}$  C.), caused the dog's intestine to relax very slowly and gradually, but the cat's intestine relaxed almost at once, and this was also true when the undiluted liquid esters were injected. The cat is apparently an exception to the rule formulated by Macht (J. Pharm. & Exper. Therap., 2:427, 1918) on the difference between the carnivora and herbivora in regard to benzoic acid metabolism.

(1c-15)

(1c-16)

(1c-17)

(1c-17)

**Experimental Research on the Influence of Chlorophyl on Cardiac Function.**

*Koichi Miyadera, Berl. klin. Wchnschr., 58:1159, Sept. 26, 1921.*

Burgi declared that gastric alimentation of pure chlorophyl has a strengthening and a sedative effect upon the action of the heart, and demonstrated his theory by curves which he obtained by flame cardiography. As pure chlorophyl is only soluble in fatty substances, certain difficulties present themselves when experimenting upon animals, for fat embolism occurs after intravenous injection of solutions of chlorophyl in olive oil. Miyadera exposed a frog's heart, fixed to the apex the threads of an Engelmann's heart-lever and then attached a kymograph. Every twelve seconds a drop of the solution dripped on the heart and irrigated it. In control experiments, pure olive oil remained ineffective during one and a half hours' observation; sometimes a slight bradycardia occurred, alternating with normal or slightly accelerated heart action. Solution of 5 gm. alcoholic chlorophyl extract in olive oil, without any noticeable alcoholic content, was used, a dark room excluding any photo-dynamic effect. Application of previously warmed, then cooled solutions every five minutes, registered slight bradycardia as the regular effect of chlorophyl on the heart. The diastole was protracted, the elevation was frequently exaggerated. This last aspect was wanting in a more pronounced bradycardia.

(1c-18)

(1c-18)

**Experimental Inquiry into the Cerebral and Neuromuscular Manifestations of Digitalis.**

*D. I. Macht, Arch. Int. Med., 28:678, Nov. 15, 1921.*

Duroziez observed 20 cases of delirium or hallucinations which he attributed to digitalis; in some of the cases death followed. The experiments of Macht were carried out with albino rats, and the phenomena following administration of digitalis were tested by the behavior of the animals in a circular maze. In every instance the rats had made 3 exits from the maze, without mistakes, while normal. The drugs selected were then injected, intraperitoneally or intramuscularly, and the effects noted at intervals of one hour after administration, several hours afterward and on subsequent days, until either death or recovery occurred, the latter in cases of small dosage. Effects of the following drugs were studied: oubain (or crystalline strophanthin), Merck's amorphous strophanthin (Kombé), digitoxin, digitonin, digitalin (various samples), digalen, and several injectable preparations of digitalis leaf, such as digitoxin, digipuratum and digifolin. A few experiments were also made with bufagin, the drug, related to the digitaloids, which Abel isolated from the skin secretions of toads. The results of the series of experiments accord with the conclusions of Duroziez. The various digitaloids, even when given in comparatively small doses, had a depressant effect upon the behavior of the animals. Whatever theory one may hold in regard to the psychologic data furnished by the maze problem, it will be generally conceded that the effects produced by the drugs must be referred for the most part to the central nervous system and, at least to some extent, to its higher centers.

(1c—19)

**Comparative Experimental Studies of the Effect of Various Heart Remedies.**

*Julius Citron, Deutsch. med. Wchnschr., 47:1285, Berlin, Oct. 27, 1921.*

Up to the present all heart remedies have been placed on the same level, owing to the fact that the experimental administration of fatal doses of all the preparations of the digitalis group (digitalis, adonis, convalleria, and strophanthus) led to systolic heart failure. A heart which is unaffected by digitalis, can be influenced by adonis, indicating that the protoplasm of the heart muscle, in addition to the chemoreceptors for digitalin, must also have others for Adonis vernalis.

Citron experimented with adonidin and digipuratum and made electrocardiographic records. Preparations of strophanthus and zymarin (similar to adonidin) were also tried. For the electrocardiographic examination of frogs' hearts, digitalis-like substances must be divided into three groups: (1) digipuratum, (2) adonidin, and (3) tincture of convallaria majalis. Strophanthin contains chemoreceptors of the digipuratum and adonidin group. Zymarin belongs principally to the adonidin group. Calcium chlorid, the mechanical effect of which is similar to that of digitalis substances (systolic heart failure), potassium chlorid and quinin were also tested. The electrocardiograms of an isolated frog's heart after the application of the different remedies of the digitalis group having the same mechanical effect were entirely dissimilar, proving that contraction is influenced in different ways. Digipuratum decreases the auricular beats per minute. Adonidin lengthens the auriculoventricular conduction time, leaving the distance between the apices of the auricular waves unchanged. Tincture of convallaria quickens auriculoventricular conduction and, in large doses, tends to lessen the distance between the auricular waves. Calcium chlorid increases the distance between the auricular waves and shortens the *J* wave. The *J* wave (*R* wave according to Einthoven) becomes much smaller. Calcium chlorid greatly increases the distance between the auricular waves, slightly prolongs the *J* wave and causes splitting of the *J-p* wave. Quinin hydrochlorid causes a deep splitting of the *J-p* wave. When several drugs act on the same heart the characteristic curve for each can be seen. All heart remedies are not alike in their effects. By dint of continued experimental and clinical study it will be possible to progress from a routine plan of action to individual treatment based on biologic principles.

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(1c—20)

**Eukupin.**

*Eduard Boecker, Deutsch. med. Wchnschr., 47:1253, Berlin, Oct. 20, 1921.*

A study, similar to that of the quinin content of the lungs and sputum in pulmonary tuberculosis, has been made on eukupin. After it is given by mouth, to patients with tuberculosis, it appears in the sputum. There would doubtless be a more pronounced excretion if it were given parenterally. After ingestion, it was also found in tuberculous lungs. When there was a mixed infection of tuberculosis with streptococci or staphylococci, eukupin had no therapeutic effect.

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(1c—20)

(1c-21)

**Quinin Distribution in the Body.**

*E. Boecker, Deutsch. med. Wchnschr., 47:1201, Berlin, Oct. 6, 1921.*

According to Aufrecht the course of croupous pneumonia is very favorably influenced by the subcutaneous administration of quinin muriate, preferably in doses of 0.5 gm. in a 10% solution with 5% urethan. The author therefore made a study of the quinin content of the sputum of patients and the lungs of animals that had been given quinin parenterally. A considerable amount of quinin appeared in the sputum of the tuberculous patients. The lungs of guinea-pigs showed a considerable quinin content; the liver, which weighs  $4\frac{1}{2}$  times as much, contained only three-fifths the amount found in the lungs. Doubtless there is a certain affinity of the lung tissue for quinin. The lungs, as well as the kidneys, and salivary and sweat glands play a part in the excretion of quinin from the body.

(1c-21)

(1c-22)

**The Action of "Bayer 205" on Trypanosoma Equiperdum in Experimentally Infected Mice.**

*C. M. Wenyon, Brit. M. J., London, Nov. 5, 1921, p. 746.*

A sample of this drug was tested on a virulent strain of *T. equiperdum* in mice. The animals were inoculated intraperitoneally from another heavily infected animal. The drug was given forty-eight hours afterward by the intravenous route when trypanosomes were swarming in the blood. After varying doses, it was found that a dose of 0.005 gr. per kilogram of body weight produced an apparent sterilisans magna; no relapses followed; the mice were healthy. In every instance (over 50 mice) a single injection of a suitable dose brought about a sterilisans magna; so probably this drug, whatever may be its constitution (this has not yet been made public), will be found to be a more efficient remedy than those hitherto used in cases of human and animal trypanosomiasis. Other remedies tested did not produce permanent cures with single doses; animals relapsed and died of their infection. The dosage of "Bayer 205" for man must be determined by direct trial, as calculations based on animal dosage are full of fallacies; this is now being done. Different samples of the same drug may vary in their action, but since tests show its remarkable trypanosomicidal action, the drug should be tried in naturally occurring cases of human and animal trypanosomiasis, to discover whether it will have in these as definite an action as in that produced experimentally in small animals.

(1c-23)

**The Study and Experimental Therapeutics of Heat-Stroke.**

*C. Ricket, Jr., Compt. rend. Soc. de biol., 85:713, Paris, Oct. 22, 1921.*

Experiments were made with mice and rats. The animals, placed in glass jars, were exposed to the sun and to the dry heat in an oven. Thermic, and not luminous, rays produce death (6 confirmatory tests). New-born or very young mice are less resistant than adults. Adolescent mice resist better than adults. The resistance of adult individual mice varies. Fasting rats and mice, and those which have been bled, resist less than normal animals. Physical treatment, as ventilation and tepid applications, is useful. Ether, alcohol, morphin, adrenalin and kola are  
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(1c-23)

seemingly without effect. Two drugs appear unmistakably effective, namely, caffeine and camphorated oil; by these life was prolonged in 40% of the cases. The dosage, conditions and results are tabulated.

(1c—24)

**The Action of Organ Extracts on Blood Pressure.**

*H. Roger, Presse méd., 29:901, Paris, Nov. 12, 1921.*

Having first recalled some technical points concerning blood pressure experiments on animals, the writer mentions the controversy regarding the rôle of adrenalin, which is considered by Gley as a useless and dangerous product of excretion. Some facts which tend to show that adrenalin has a physiological importance are reported. If an injection is made with blood from the veins of the adrenals, a rise of blood pressure is observed, but when the splanchnic nerves are stimulated at the time that blood is collected from the adrenal veins, the hypertension obtained from its injection is much more considerable than before.

In various pathological or physiological conditions when the blood pressure tends to decrease, an excess of adrenalin is thrown into the circulation. For instance, stimulation of the vagus in a normal animal produces a fall of the diastolic blood pressure lasting six or eight seconds; even when the stimulation is kept up the heart continues to beat, while in animals deprived of their adrenals the heart under these conditions is stopped for thirty to sixty seconds. Likewise, if adrenalin is injected at the same time that the vagus is stimulated, the characteristic fall of blood pressure does not take place, adrenalin having rendered the heart insensitive to the inhibitory action of the pneumogastric.

It is probable that many glands are capable of modifying the blood pressure. This is the case with the thyroid and hypophysis from which an active and crystallizable substance has been isolated. It is also probable that all cells of the body pour into the circulation substances which modify the blood pressure. It is doubtful, however, whether the albumins which are produced by the ordinary processes of maceration or freezing methods ever escape from the cells under physiological conditions. In order to approximate normal conditions as far as possible the author has been making use of autolyzed extracts, for it is known that processes of autolysis occur constantly in the organism and by this means substances having a small molecule are thrown into the circulation.

The action of pulmonary extracts obtained by simple maceration was first studied. These produce a decrease in the blood pressure when the extract is fairly concentrated, which may be due to the fact that colloidal substances have a hypotensive effect when they are used in sufficient concentration. This may be sufficient to offset the specific hypertensive action which is revealed when very dilute solutions are used. As a matter of fact extracts obtained by prolonged autolysis, instead of maceration, produce an extremely marked rise of blood pressure. Liver extracts were also shown to have similar properties. The kidneys on the other hand give rise to hypotensive substances by autolysis. Concurrently with the decrease of blood pressure the contractions of the heart become very slow and strong. When the injection is finished the pressure rises and becomes higher than normal, while the pulse pressure may reach 15 to 20 mm., as compared with 2 mm. before the injection. The use of autolyzed extracts renders these experiments somewhat difficult.

for putrefaction sets in very easily through accidental contamination of the tissues and when antiseptics are used a foreign element is added which may vitiate the results. For these reasons Roger has made use of extracts obtained by hydrolysis in a 3% solution of sulphuric acid heated to 120° C. for one hundred hours. The liquid which is obtained thus is freed from peptones, neutralized and extracted. With this extract results are obtained which are quite similar to those produced by stimulation of the pneumogastric, although the fall of blood pressure is somewhat less sudden. It is also noted that successive injections may stop the heart suddenly and permanently which fact is of special interest when it is remembered that diseases of the kidneys sometimes produce sudden death. The same results are obtained when the pneumogastric nerves are severed in the cervical region but the effect of the kidney extract is inhibited by atropin. Its action therefore probably takes place on the endings of the vagus fibers in the heart, according to accepted ideas as to the effect of atropin on these endings. This is, however, subject to criticism and further experiments should be made to ascertain whether the action of the kidney extract may not take place through His' bundle or at least through its sinus origin.

It is not yet known whether the substance in question exists in the kidneys or whether it is produced by the manipulations made necessary for its isolation, although Roger is inclined to believe the former, since it is also found in the autolytic products of the kidney. The fact that a renal product has been found which seems to act on the pneumogastric as adrenalin does on the sympathetic is interesting; it may be made use of to explain certain symptoms observed in diseases of the kidneys and will perhaps also find therapeutic applications.

(1c-25)

**Critical Examination of the Biologic Dosage of the Hypertonic Principle of the Hypophysis.**

*L. Stern and R. Peyrot, Compt. rend. Soc. de biol., 85:804, Paris, Nov. 5, 1921.*

There has been lack of uniformity in results obtained in experiments with organic preparations on smooth muscle. Recent work by Tredelenburg and Borgmann indicates that there is a constant relation between the effects of histamin and a preparation of hypophysis on the uterus of the guinea-pig. The authors' experience did not show this result. A study of the question was made by comparing the minimum doses of a 1:1,000 solution of histamin hydrochlorate and 3 preparations of hypophysis which caused increased tone of the uterine muscle in guinea-pigs. The effective dosage varied considerably with the four substances examined. There is no constant relation between the effects of histamin and of the different preparations of hypophysis. Standardized doses of hypophyseal extracts are not practicable, as has been claimed. The effects probably vary because of impurities.

(1c-26)

**The Influence of Pituitrin on Blood-Sugar.**

*A. Partos and Frieda Katz-Klein, Ztschr. f. d. ges. exper. Med., 25:98, Berlin, Oct. 14, 1921.*

The contradictory findings obtained by different authors, in connection with this question, are probably due to the fact that no attention was  
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(1c-26)

paid to the dilution of the blood which takes place under the influence of pituitrin. This may conceal a considerable increase in the amount of sugar in the blood, and it is therefore necessary, in these experiments, to determine the dry residue and to calculate the percentage of sugar.

The authors used for their experiments rabbits which had been fed carrots, but had received no food on the day of the test. After the blood-sugar had been determined, the animals were inoculated subcutaneously with from 0.8 to 1 c.c. of Heisler's pituitrin, and the blood-sugar titer was observed for several hours. The percentage of blood-sugar remained unchanged, but when it was reckoned on the basis of the dry residue, an increase was noted, once of 31.9%, again of 27.4%. No glycosuria was noted. If, owing to dry feeding for from two to four days before the test (only oats, and no water), the animal body did not contain enough fluid to produce hydremia, pituitrin had little influence on the concentration of the blood, and an increase in sugar could be directly demonstrated. Since bilateral division of the splanchnic nerve did not affect the action of pituitrin on the increase of sugar, this must be of peripheral origin; an injection of caffein, which acts centrally, did not produce hyperglycemia after division of the splanchnic nerves.

To determine the effect of the pituitrin injection on adrenalin glycosuria, the authors studied, first, the effect of an adrenalin injection, repeated after several days, on the sugar content. They encountered differences of 20-25%, which are within the limits of error and therefore prove nothing. In the adrenalin-pituitrin experiments, adrenalin was injected subcutaneously, and the blood-sugar titer was controlled for from six to ten hours. Six to ten days later, the same animal was injected (in another region) with the same amount of adrenalin (0.34 mg. per kilo body weight), and from 2 to 6 c.c. pituitrin, also subcutaneously. Again the sugar titer was observed for from six to ten hours. A certain antagonism between adrenalin and pituitrin was noted, evidenced by the fact that the amount of blood-sugar was decreased by increasing doses of pituitrin. Adrenalin hyperglycemia was not completely inhibited. Part of this inhibiting action is to be explained by an altered amount of dry residue.

Theobromin hyperglycemia, however, was not influenced by pituitrin, as the authors demonstrated, in opposition to the claims of Stenström.

(1c-27)

**The Effect of Adrenalin upon Respiration.**

*Ff. Roberts, J. Physiol., 55:346, London, Nov. 18, 1921.*

Experiments on rabbits and cats were made to determine the cause of the respiratory variations produced by adrenalin. The animals were given a preliminary dose of urethane and the anesthesia continued by C.-E. mixture. Respiration was recorded by connecting one limb of the Y-shaped trachea-tube to a thin rubber tambour, the other limb being open to the air. A blood-pressure cannula was tied into one of the carotid or femoral arteries. The injections were made through cannulas into either jugular vein and sometimes into the distal end of the carotid or vertebral artery. The dose was commonly 1 c.c. of 0.01% adrenalin. Graphs show that the adrenalin caused not only a diminution and temporary arrest of respiration, but also an alteration in rate, and in some cases Cheyne-Stokes respiration. That such respiratory modifications  
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(1c-27)

were not entirely due to the increased blood-pressure which accompanies adrenalin administration, was proved by connecting the animal's aorta with a "blood-pressure compensator," a device which eliminates considerably blood-pressure changes. Nevertheless, following adrenalin injection the change in respiration, though not as intense as it was without the compensator, was very marked and always much more prolonged. That adrenalin does not directly or indirectly inhibit the respiratory center by nervous impulses from the periphery was determined by experiments in which the central end of the splanchnic was stimulated, or the abdominal aorta ligated below the origin of the celiac axis and adrenalin injected below the ligature, or in which the vagi were divided. By a process of elimination it is concluded (and is proved experimentally) that the respiratory variations produced by adrenalin are caused by sudden anemia of the respiratory center due to vasoconstriction.

(1c-28)

(1c-28)

**Effect of Adrenalin on Healthy Persons.**

*Alfred Bjure and John Svensson, Upsala Läkaref. Förh., 36: No. 6, Stockholm, Sept. 1, 1921.*

Since 1917 the authors have conducted experiments for the purpose of examining the reactions of healthy persons to adrenalin. They also examined the effect of the preparation on individuals with evident anomalies in the functions of different organs of internal secretion. Several reactions due to the remedy were studied simultaneously, such as the effect on blood-pressure, pulse, respiration, blood-sugar, hemoglobin, red and white blood-corpuscles, diuresis and NaCl concentration in the blood and urine. Tremor, symptoms of subjective disturbances and the dermography were also observed. The experiments were performed on 5 healthy medical students; 3 experiments were made on each student, 1 control test and 2 tests with injections of 0.5 and 1 mg. of adrenalin, respectively; the same solution of adrenalin was employed in each test. The following results were obtained: Both the intramuscular and the subcutaneous injections of adrenalin had the same effects. The blood-sugar value rose to maximum three-quarters of an hour after the injection, and a maximum lymphocytosis was observed half an hour after the injection. In a great majority of cases a rise in the blood-pressure was also observed about half an hour after the injection. The respiration changed but little and had a tendency to increase. In only 1 case out of 10 was there evident a persistent increase in the hemoglobin and in the number of red blood-corpuscles. In other experiments the changes in this respect varied. The quantity of urine was often increased and thereby the absolute quantity of NaCl, although the NaCl concentration decreased. In other cases the result was reversed. It was not possible to determine whether or not the percentage of NaCl in the blood changed; the authors believe, however, that the percentage sinks about three-quarters of an hour after the injection. Comparisons between the same reactions in different persons and between the various reactions in the same individual give widely varying results. The authors observed an evident tendency to a relation between some reactions, such as the blood-pressure, blood-sugar and lymphocytes. In a great majority of the cases the effect of adrenalin was more marked after the injection of 1 mg. than was the case after the injection of 0.5 mg. In other cases the results were exactly reversed, at least in respect to some of the reactions.

(1c—29)

(1c—29)

**Researches on Adrenalin Hyperglycemia.**

*Ch. Achard, A. Ribot and Leon Binet, Rev. de méd., 38:447, Paris, Sept., Oct., 1921.*

In the experiments reported here hyperglycemia was produced in dogs by intravenous injections of glucose and its variations were studied when adrenalin or organ extracts were administered at the same time. Quantitative analysis of the blood sugar was made by Epstein's method. From experiment on 5 normal dogs it was ascertained that when 0.50 gm. glucose per kg. is injected, the hyperglycemia lasts about twenty minutes, and twice as long when 1 gram per kg. is given.

In another animal glucose and adrenalin were injected simultaneously and separately. The results show that the addition of adrenalin to glucose produces a more considerable glycemia than either glucose or adrenalin alone. Furthermore, the effect is protracted. It is as though the organism under the influence of adrenalin becomes unable to fix or to burn sugar. Similar results were obtained with hypophyseal extracts.

The various pancreatic extracts found in the trade do not possess glycolytic properties, although freshly prepared extracts do produce a reduction of the blood sugar. An experiment, made to ascertain the effect of this extract when injected at the same time as glucose, showed that under these conditions the glycemia is less intense and of about half the duration as when no pancreas extract is injected. Furthermore the transitory hyperglycemia is followed by a decrease in the blood sugar for a long time. Adrenalin inhibits the action of pancreatic extract when both are injected together in similar experiments. An antagonistic action was also shown to exist between hypophyseal and pancreatic extracts. Finally when adrenalin is injected in a pancreatectomized dog, the hyperglycemia is not increased. Apparently adrenalin has no further influence on sugar metabolism when its inhibitory action on the internal secretion of the pancreas cannot take place.

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(1c—30)

(1c—30)

**Action of Renal Extracts on the Pneumogastric Nerve.**

*H. Roger, Compt. rend. Soc. de biol., 85:710, Paris, Oct. 22, 1921.*

It is usually supposed that the cells produce substances which, escaping into the blood, modify pressure by acting on the vessels or heart. Objection to this view depends on the fact that the extracts employed are ready-made, or are prepared by macerating finely divided tissue in cold saline solutions, or by pressure, or by alternate freezing and thawing. The liquid obtained is invariably rich in albuminous cell-constituents which probably do not escape into the blood physiologically. The author, by using autolyzed tissue extracts, has obtained results that differ from those usually obtained. Macerated liver or lung tissue supplies a hypotensor substance, which also slows and strengthens the systole; as its effects gradually fade, there is slight rise above normal tension and oscillation to the normal, with diastolic-systolic oscillations of remarkable slowness and amplitude. The effects recall vagus stimulation. Perhaps the kidney contains a substance affecting the tenth nerve, as adrenalin does the sympathetic. The autolytic method is delicate, and decomposition occurs readily; the chemical method is better than the tests complicated by the uncertainties of antiseptics.

The finely divided tissue is mixed with 1.5 its weight of water acidulated with 3% sulphuric acid. For 100 hours it is maintained at 120°, then filtered, neutralized with barium oxid, treated with mercuric chlorid, the excess of mercury being removed by hydrogen sulphid, concentrated in vacuo and precipitated with alcohol. The alcoholic extract is redissolved in water and injected intravenously into dogs and rabbits. If the concentration is sufficient, the effect suggests faradic vagal stimulation, the fall of pressure being a little less abrupt; it may be 6-7 cm., the heart-beat becoming slow and full. With more dilute extract, the fall is not so marked, but the beat is very energetic. In one test, on the rabbit, pulsations fell from 200 to 74, the amplitude increasing from 4 mm. to 2.5 cm. Successive injections augment the intensity. Fatal syncope may result in the rabbit, with sudden arrest of the heart in diastole, respiration ceasing a few seconds later. Results are the same after section of the two vagi. The renal substance, therefore, does not act upon bulbar centers of the vagus. Results are different after intravenous injection of neutral atropin sulphate. A small dose suffices. Instead of falling, the pressure is slightly raised. A larger dose entirely abolishes the renal extract effect, and twice the amount usually producing fatal syncope may be introduced without result. The renal parenchyma is believed to contain a substance which acts on the cardiac terminations of the vagus, and the effects of which are prevented by prior injection of neutral atropin sulphate.

(1c—31)

(1c—31)

**The Comparative Effects of Parathyroid and Thyroid Feeding on Growth and Organ Hypertrophy in the White Rat.**

*A. T. Cameron and J. Carmichael, Am. J. Physiol., 58:1, Nov. 1, 1921.*

Four series of experiments were performed on white rats which were fed on unlimited quantities of bread and milk. In the first three experiments desiccated beef parathyroid (iodin-free) was fed daily in doses bearing fixed ratios to the actual weight of the animal, corresponding doses of desiccated beef liver being fed to control animals. In the final experiment a direct comparison of the effect of the parathyroid powder and of thyroid was made. The desiccated hog-thyroid contained 0.34% iodin. In all cases the parathyroid powder was mixed to a paste with water and flour and fed shortly after weighing the animal each morning. At the end of each experiment the animals were killed and immediately dissected, and the organs were transferred to closed glass vessels and weighed. The tabulated results indicate a possible decrease in growth rate from feeding parathyroid, unaccompanied by any apparent hypertrophy except of muscle. Such was the case in one experiment, but the remaining experiments did not confirm this decrease. There were somewhat greater variations than usual in the rate of growth, but no effect resembling that of thyroid fed in much smaller doses for similar periods. In general the results indicate that even very heavy doses of parathyroid produce no definite effect on growth and no organ hypertrophy. Of the animals fed thyroid, 6 developed marked tetany. The underlying causes of the latter condition will be discussed in a subsequent paper.

(1c—32)

**The Effect of Thyroid Feeding on Growth and Organ Hypertrophy in Adult White Rats.**

*A. T. Cameron and F. A. Sedziak, Am. J. Physiol., 58:7, Nov. 1, 1921.*

It was endeavored to ascertain if the hypertrophy of lymphoid tissue as well as the hypertrophy of other organs follows the administration of thyroid to adult white rats. Accordingly from March 4 to March 22 a daily dose of thyroid in the ratio of 1:5,000 of actual body weight, was fed to each of 7 rats, other rats being used as controls. All of the animals were fed unlimited quantities of bread and milk. At the end of eighteen days the rats were killed and the organs were dissected and weighed. The tabulated results show that even in adult rats the administration of thyroid produces a distinct retardation of growth. While the treated rats show a loss of weight, the controls show a slight gain. Nevertheless, while the weight of most of the treated animals was lower, the weight of the kidneys, heart, spleen, lymph glands and adrenals was actually greater in the treated animals.

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(1c—33)

**Variations of the Blood Formula Produced by Extract of Lymphatic Glands, with Special Reference to Eosinophilia.**

*Arturo Mazzarella, Riforma med., 37:1103, Naples, Nov. 19, 1921.*

Wherever experiments have been made with "lymphoganglina," a marked depression has been noted in the sympathetic system which we must recognize as a vagotonia. Mazzarella made experiments which confirmed earlier researches, in which he showed that the blood formula was constantly modified with increase of lymphocytes and of eosinophils. Pilocarpin produced eosinophilia, but with different time and intensity from that provoked by "lymphoganglina." Adrenalin produced exactly opposite results; notably, increase of polynuclear neutrophils and disappearance of eosinophils. The extract of lymphatic glands besides increasing white corpuscles, modifies the formula, producing mononucleosis and especially eosinophilia; the latter differs greatly from the familiar eosinophilia of serum, and hence cannot be confused with it; it differs also from that eosinophilia which is obtained by directly exciting the vagus (pilocarpin), the latter being quicker, more intense and of less duration; the observations of Marfori and Christoni are confirmed, i. e., that the extract of lymphatic glands exercises an action of a hormonic nature, opposite to that of adrenalin, and hence depresses the sympathetic nervous system.

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(1c—34)

**Animal Experiments with Placenta Opton.**

*Kratzeisen, Deutsch. med. Wochenschr., 47:1260, Berlin, Oct. 20, 1921.*

Virgin guinea-pigs 4 weeks old, were fed 0.5 c.c. of 5% placenta opton extract every two days, and were killed after they had received 30 c.c. The autopsy findings showed definite enlargement of the mammae and nipples. The uterus and vagina were increased to double the size, thickness and width of those of the control animals. The difference in sexually mature animals was even greater. The uterus was

hypertrophied. Parenchymatous nephritis was found by other authors in similar experiments, but has not been observed in Krazeisen's experiments.

(1c-35)

(1c-35)

**Fixation and Neutralization of Poisons on the Nervous Centers.**  
*Jean Camus, Bull. Acad. de méd., 86:302, Paris, Nov. 29, 1921.*

For several years the author has studied the fixation of poisons by the nervous centers when various substances are injected in the cerebrospinal fluid of animals or directly into the brain. Some poisons (lead, tetanus toxin) act only after a certain incubation period. Most, however, produce their effects immediately. A number of chlorids and sulphates were studied. In a general way the rarer salts are the most toxic. The toxicity of a substance should be based on the number of molecules injected.

The fixation of poisons and their action is influenced by the state of the meninges at the time. If, for instance, an aseptic meningitis is produced in an animal, the intravenous injection of lead, which would be otherwise harmless, produces the same effects as if it were injected directly into the cerebrospinal fluid. Certain poisons have particular affinities. Very feeble doses of chloralose, for instance, excite the vomiting centers, while slightly higher doses paralyze them; the other vital centers remain intact. Attempts at neutralization were made with antagonistic substances and chemical antidotes. An example of antagonism is given by the slowing of feverish polypnea produced by pilocarpin, the action of which is neutralized by atropin. The syncopal attacks produced by spinal injections of stovain, or syncain may be warded off by caffeine, which has, however, no power to neutralize a lethal dose of these anesthetics. Tetanus antitoxin injected into the cerebrospinal fluid is the best means of treating frank tetanus; this is probably due to the fact that further fixation of the toxin is prevented, not to neutralization of that which has already been fixed by the nervous centers. From this and other experiments it does not seem possible to neutralize *in situ* a poison which has been rapidly and securely fixed by the nervous centers, but the effects of these poisons may nevertheless be successfully fought in certain circumstances.

(1c-36)

(1c-36)

**The Peril of Wood-Alcohol Toxemia and the Remedy.**  
*S. Lewis Ziegler, Pennsylvania M. J., 25:177, Dec., 1921.*

Three factors should induce manufacturers to abolish the use of wood-alcohol and substitute denatured alcohol: humanitarism, self-interest and practical economy. Most of the wood-alcohol in the body is eliminated by the lungs, skin, kidneys and alimentary tract, while the remainder undergoes oxidation into formaldehyd and later formic acid, both of which exert a corrosive action on living tissues. Even where small quantities have been absorbed, as by wood-alcohol workers, there is enough formic acid excreted in the urine to reduce Fehling's solution. This fact is of great importance, as the presence of sugar might thus be suspected, and diabetes falsely diagnosed, especially if there were associated ocular lesions. Since acidosis is a constant factor in the early stages, intravenous injections of sodium bicarbonate should be given promptly, the indications being governed by Van Slyke's test

for the carbon dioxide in the blood. Caution is necessary, as excessive alkalosis may cause grave irritation of the kidney. On the other hand, in the later stages of 1 case a marked alkalosis of 113% promptly yielded to treatment. In mild cases of toxemia, sodium bicarbonate, 20 gr. should be given every two hours. Donovan's solution will prove most efficient as an active eliminant. Pilocarpin will stimulate lymphatic activity. Additional eliminative treatment, i. e., lavage, emetics, dia-phoretics and rapid oxidation, has proved of value. The optic nerve should be stimulated by applying negative galvanism. Strychnin has not proved successful in the writer's hands. A practical method for the testing of suspected liquids for wood-alcohol is by converting the wood-alcohol, by oxidation with potassium permanganate, into formaldehyd, then adding it to acidulated milk and gently heating until a pink color develops. This test is so delicate that 0.01% of methyl alcohol may be detected.

(1c—37)

(1c—37)

**The Effect of Hydrogen-Ion Concentration on the Toxicity of Alkaloids for Paramecium.**

*Marian M. Crane, J. Pharmacol. & Exper. Ther., 18:319, Dec., 1921.*

The limits of hydrogen-ion concentration within which paramecium can live twenty-four hours have been found to be approximately 1 by 10-9.6 and 1 by 10-5.0. The magnitude of the effect upon toxicity of definite changes in hydrogen-ion concentration has been determined for a number of alkaloids. The effect of changes in hydrogen-ion concentration upon toxicity has been found to vary with the dissociation constant of the base. The free, undissociated base is apparently responsible for the toxicity. The effect of hydrogen-ions upon toxicity is evidently due to an action upon the drug. If there is any direct action upon the resistance of the cell, it is very slight at the concentrations studied.

(1c—38)

(1c—38)

**Passive Shock in the Guinea-Pig Produced by Intracardiac Injection of the Serum of Animals Intolerant of Arsenobenzene.**

*A. Tzanck, Compt. rend. Soc. de biol., 85:839, Paris, Nov. 12, 1921.*

Since 1913, the author has attempted to produce passive anaphylaxis by injecting serum of guinea-pigs intolerant to arsenobenzene, and following this, on the same or the subsequent day, with an injection of arsenobenzene. Heretofore he has made subcutaneous or intraperitoneal injections without results. Results have now been obtained by intracardiac injection of 1 c.c. of the serum of the animal (guinea-pig) intolerant to novarsenobenzol, and 1 cg. of sulpharsenol, which produce an anaphylactic crisis in about three minutes from which the animal completely recovers in a few minutes. The phenomenon does not occur after injection of the serum or salt alone.

(1c—39)

(1c—39)

**A Toxic Series of Novarsenobenzol.**

*Ch. Laurent, Bull. Soc. franç. de dermat. et de syph., Paris, No. 8, 1921, p. 367.*

Twelve injections of novarsenobenzol were given the same day by  
(Sec. 1—Page 86)

the same physician under identical conditions, except that in three a preparation was used which belonged to a series of manufacture designated as No. 12,944. Serious accidents occurred in all three cases and death appeared imminent in one. This last patient had previously received somewhat smaller doses without trouble. Almost immediately after the injection of 0.60 gm. of novarsenobenzol of the toxic series, the patient became extremely red in the face, was seized with convulsions and his pulse became imperceptible. Recovery followed only after several hours after a subcutaneous injection followed by intravenous administration of adrenalin. The other two patients had similar but less serious symptoms. One had had a nitritoid crisis previously, because of which adrenalin had been administered preventively before the second injection. Nevertheless 0.30 gm. of novarsenobenzol of the 12,944 series produced a very serious crisis immediately.

These accidents confirm similar experiences by other authors. The manufacturers express astonishment in such cases and give assurances that animal tests have yielded perfect results, but this cannot be considered a satisfactory explanation.

(1c-40)

**Poisoning with a Benzine Substitute, Benzinoform.**

*Freyymuth, Berl. klin. Wchnschr., 58:1330, Nov. 7, 1921.*

Benzin, benzol and benzinoform are not chemically related. Benzin is an aliphatic substance; benzol belongs to the aromatic series; the benzin substitute, sold as benzin fluid under the name benzinoform, is tetrachlormethane or carbon tetrachlorid. An inflammable liquid (trichlormethane) is similar to chloroform. In a case of poisoning reported by von Curtius tetrachlormethane was isolated from the body. Tetrachlormethane has a stronger narcotic effect than chloroform and produces death through paralysis of centers in the medulla, while benzol causes death by suffocation. The pulmonary edema found by von Curtius in his case was a secondary phenomenon. Benzinoform should be withdrawn from unrestricted sale and the public informed of its poisonous effects.

(1c-41)

**A Case of Creosote Poisoning in an Infant.**

*Ivar Thorling, Upsala Läkaref. Förh., '36: No. 34, Stockholm, Sept. 1, 1921.*

The patient, a boy aged 2 months, was brought to the hospital suffering from creosote poisoning. At 7 a. m. on the same day the boy's mother had given him a quantity of creosote by mistake. It was not possible to determine the amount, but the author thinks that it was probably about 0.6 c.c. The mistake had been observed immediately after the administration of the poison and the child's mouth had been washed with warm water. About one hour after that, the mother tried to nurse the child, but he vomited immediately after having swallowed a few drops of milk. A new, spontaneous attack of vomiting occurred in the afternoon; the child had been restless during the day. At 5 p. m. the stomach of the infant was rinsed, and one hour after that the child was brought to the hospital. On his arrival, he was conscious but seemed to be in a very poor condition. His skin was pale gray in color, lips cyanotic and on his lips and in his mouth numerous eschars were found.

(1c-41)

The temperature was 37.8° C. and the pulse 165. The heart-sounds were normal and audible. The feces were grayish-brown, solid and homogeneous, and smelled of creosote. The Weber reaction in the feces was negative. The urine was dark grayish-brown. The blood had a peculiar, dark color and a somewhat thick consistence. The number of red blood-corpuscles was 1,800,000 and that of the leukocytes was 25,-600. On the following day the temperature was 39.2° C. and the pulse about 170. The eschars in the mouth loosened. The infant was icteric, pale, and cyanotic. The breathing was dyspneic and groaning. The guaiacal reaction was positive. On the third day the temperature was 38.4° C. in the morning and 38.3° C. in the evening. The pulse was 170 and respiration 64. The icterus was pronounced and the child was extremely pale, his lips cyanotic. In the afternoon the condition grew worse and the eyes became glassy. Ptosis was observed in the left eye. The feces were loose and dark. The Weber reaction was still negative. About 6.30 p. m. on the third day the child became comatose, with steadily slower breathing and reduced cardiac frequency. He died at 7 p. m. on the third day following the poisoning.

(1c-42)

Hemorrhages within the Cardiac Muscle in a Case of Poisoning with Illuminating Gas.

*Georg Strassmann, Wien. klin. Wchnschr., 34:483, Oct. 6, 1921.*

A family of 4 persons was affected, 3 of whom recovered, a youth of 18 succumbing without regaining consciousness. He was probably never robust. Autopsy showed hypoplasia of the vascular system, enlarged thymus, enlarged tonsils, numerous large pharyngeal follicles, spleen enlarged with a deep notch, the appendix elongated, sigmoid elongated and very movable, upper epiphysis of the humerus persistent. Possibly these constitutional conditions were responsible for the death. Heart findings: hypertrophy of right and slight hypertrophy of the left ventricle; valves intact. Under the pericardium there were diffuse, confluent hemorrhages over a large portion of the upper surface of the heart, extending deep into the muscle and penetrating entirely the cardiac wall in certain areas about the right ventricle. Histologically there were accumulations of polynuclears, and especially erythrocytes in the epicardial fatty tissue, in the epicardium and in the connective tissue lying between muscle bundles; the muscle fibers were crowded apart by the red cells. Only 1 other such case is recorded (Liebmann). In the present case it is possible that preexisting disease of the cardiac muscle predisposed to the extravasation of blood which occurred.

(1c-43)

Carbon Monoxid, Illuminating Gas and Benzol. Their Effect on Blood Coagulation Time.

*Henry S. Forbes and Louise Hompe, J. Indust. Hyg., 3:213, Nov., 1921.*

Pathologists disagree as to the influence of carbon monoxid on the coagulation of the blood and on the mode of action of the gas. Therefore, experiments were undertaken to determine the coagulation time of the blood of animals gassed with carbon monoxid, and to note any evidence of hemolysis. It has already been proved that this gas has no direct harmful action on nerve-cells or other tissues, but injures solely

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(1c-43)

by robbing these tissues of oxygen, by combining with the hemoglobin in the blood. Experiments were also performed with illuminating gas and with benzol, inasmuch as many cases described as carbon monoxid poisoning are due to illuminating gas, the chief toxic constituent of which is benzol.

Samples of blood (2 c.c.) drawn from cats anesthetized with urethan or ether were used as controls. Then the cats were gassed by a tracheal cannula for from thirty minutes to seven and a half hours. The percentage of vapor inhaled by the animals was not measured, but was sufficient to keep them unconscious. The experiments showed no constant change of coagulation time in the blood of cats gassed with any one of the 3 gases, and the thrombin content was apparently unaltered. Evidence of hemolysis was lacking. Clear serum was always obtained unless mechanical injury to the red-cells had occurred. The urine was never dark or smoky. Since no hemorrhages were found postmortem, it is apparent that the exact conditions of human poisoning were not reproduced, even by five hours of deep coma under the influence of the gas. The failure to reproduce hemorrhages or prolonged coma after removal from the effect of the gas may be due either to the fact that gas affects animals differently from human beings, or to the fact that the period of gassing was shorter in these experiments than in the human cases.

(1c-44)

**Lead-Poisoning, with Special Reference to Poisoning from Lead Cosmetics. Report of Four Fatal Cases of Encephalopathia Saturnina Occurring in One Family.**

*Moses Barron and Harold C. Habein, Am. J. Med. Sc., 162:833, Dec., 1921.*

Lead is the most important of the industrial poisons. Women are more susceptible to lead poisoning than men; abortions, and early fetal death are common. Lead is deposited in the liver, kidneys, brain, and other organs; it is eliminated principally through the urine and feces, but may be absent in either, even in the very severe forms of poisoning. The kidneys in some types of lead poisoning show deposits of lime salts in degenerating tubules, similar to the condition found in acute mercurial poisoning. The lesions in the brain in cases of encephalopathia saturnina are not very prominent, the principal microscopic findings being a mild perivascular round-cell infiltration, satellitosis, neuronophagia, and the occurrence around some blood-vessels of phagocytic cells containing a greenish crystalline pigment. Basophilic granulation of the erythrocytes is a striking and characteristic feature of most cases of lead poisoning, and with proper staining technic this is of inestimable value in diagnosis; careful routine blood studies should therefore be made as a prophylactic measure among the workers in industries in which lead is used. Besides being an industrial poison, lead is also the source of many miscellaneous forms of poisoning, chief among which is probably that resulting from the use of lead-containing cosmetics, the employment of which over a prolonged period of time may result in death. A face powder known as "flake white," sold quite generally in drug stores for cosmetic purposes, is lead carbonate ground to an impalpable powder. Mild degrees of poisoning from this are probably widespread, but because the symptoms are often indefinite the true etiology remains un-

(1c-44)

detected. Very severe cases probably also occur and remain undiagnosed. Four fatal cases in one family and one additional case are presented. In all of these the use of "flake white" as a cosmetic was shown to be the exciting cause. The authors urge, therefore, that rigid laws be enacted prohibiting the sale of any compound containing lead for cosmetic purposes.

(1c—45)

**Action of Mercury on the Central Nervous System.**

*H. Clément, Compt. rend. Soc. de biol., 85:855, Paris, Nov. 12, 1921.*

Treatises on toxicology contain no evidence indicating that tabes and similar symptoms observed in syphilis are caused by mercury. The author had occasion to observe ataxic symptoms said to have been caused in young men by labor in mercury mines. He reports the following results of experiments on a dog. For more than two years, the animal was given repeated doses of mercury. Comparing the average durations of human and canine life, this period represents twelve years of treatment in man. The dog weighed 17 kilos. Injections and pills were used. Gingivitis, salivation and diarrhea showed satisfactory absorption. The animal had no psychic or motor disorders.

(1c—46)

**Angina Mercurialis.**

*Johan Almkvist, Hygiea, 83:657, Stockholm, Oct. 31, 1921.*

Angina mercurialis is comparatively often overlooked or diagnosed erroneously. The condition is an unusual form of changes in the body, produced by mercury; physicians with a limited experience in mercury therapy seldom observe the disease. The clinical picture of the condition may easily be mistaken for that of some other disease. The disease is incompletely considered in the usual text-books, although its existence has been known for two hundred years. The author describes 24 cases of angina mercurialis which he has observed since 1906 in connection with the treatment of syphilis. In 2 cases the condition occurred twice. The disease may be caused by small doses in the beginning of the treatment, or at the end of a course of treatment with large doses. In 17 of the cases the angina appeared only on one side, and in 9 cases it was bilateral. In all typical cases deep furrows or sacs were observed in the middle of the infiltrate. In 15 of the cases the angina had occurred without being associated with other changes in the mouth or pharynx; in 9 cases it was associated with mercurial gingivitis or stomatitis, in 2 cases with salivation alone, and in 1 case with redness of the pharynx. Bacterial flora were found in the affected membranes in 18 of the cases, and consisted of spirochetes, cocci and *Bacillus fusiformis*. In 24 cases fever was observed and, in the 2 cases in which no fever was noted, no bacteria were found. In 5 cases the changes had spread from the tonsils into the surrounding region. The condition lasted from one to twenty-two days.

On the basis of these cases, the author came to the same conclusion as did the older authors, namely, that angina mercurialis is only a special localization of mercurial ulcerous stomatitis and is analogous to mercurial gingivitis. The spread and abscess formation of angina mercurialis is also analogous to the ulcerous process of mercurial sto-

matitis and the treatment of the two conditions is similar. Disinfection of the tonsillar crypts quickly cures the tonsillar symptoms, whenever it is possible to perform it thoroughly; in many cases it is not even necessary to terminate the mercurial treatment.

(1c-47)

**Acute Veronal Poisoning.**

*Felix Boenheim, Med. Klin., 17:1267, Berlin, Oct. 20, 1921.*

When veronal was first introduced into therapeutics, it was administered in doses up to 3.5 gm. and in daily amounts up to 8 gm. These amounts are now considered too large. Usually poisoning occurred in cases where a dose of over 10 gm. was taken, although it is known that there is an idiosyncrasy in which doses of 0.5 gm. produce serious indications of poisoning.

The most important symptoms of veronal poisoning are a more or less pronounced stupor or even syncope, instability of temperature, and vasomotor disturbances, which are always present. The patients are cyanotic with cold extremities. Despite cyanosis the breathing is quiet, superficial, and only occasionally somewhat accelerated.

Veronal affects the peripheral circulation—paralysis of the vessel wall being produced,—but no central action seems to take place. There are no symptoms of heart trouble; in most cases the pulse is unchanged and strong; occasionally it is somewhat diminished in force. There are no digestive disorders. The writer found albuminuria. Diplopia, amblyopia and nystagmus are not seen. A very remarkable change in the behavior of the pupils is observed. The pupils which shortly before were contracted, dilate, and after some time they contract again, etc. Even myopic pupils react well to light. Changes in the corneal and conjunctival reflexes take place according to the seriousness of the case. The tendon reflexes also show great instability. Abdominal reflexes are absent.

Jacobi gives an explanation of the variable picture in veronal poisoning. He describes the active principle in veronal as "a peculiar substance paralyzing the contracting tissues which are found within the capillary wall, and perhaps in the terminal arteries also, thus producing a collapse of this part of the vascular system."

In serious cases the diagnosis can be made even without a history. The most important points in the diagnosis of a serious case of acute veronal poisoning are the behavior of the pupils, that is, contracted pupils which react and absence of abdominal reflexes, while the tendon reflexes either remain normal or are increased. Urine examination confirms the diagnosis, for veronal is excreted in the urine and can be detected. The diagnosis of veronal poisoning is of no clinical value, as no specific antidote is known. Caffein is injected and the stomach washed out. The prognosis is comparatively favorable, despite the alarming symptoms. Even in cases of very large doses complete recovery is frequent.

(1c-48)

**Severe Skin Injuries Through Zyklon Vapor.**

*Seligmann, Berl. klin. Wchnschr., 58:1329, Nov. 7, 1921.*

Zyklon is a cyancarbonic acid ester which contains 10% of chlor-carbonic acid ester, a powerful local irritant, and 30% of prussic acid  
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(1c-48)

salt. The vapor, used as a disinfectant, acts on the mucous membranes of the eyes and of the respiratory system, and it is impossible to be subjected to the fumes without endangering health. Of 5 men operating a disinfecting apparatus, 3 were affected by the gas though they had no constitutional peculiarities, nor were exposed to it longer than their fellows. In one, who had rubbed the axillæ, groins and waist with methyl alcohol, smarting of these areas set in with a dry eczema and intense itching on the arms, breast and thighs and there were an edematous swelling of the scrotum and slight urethral discharge. Recovery followed in two weeks. A second patient had urticarial skin changes especially in the areas subjected to sweating and where the clothing rubbed. In this case also there was marked edema of the genitals. Recovery resulted after fourteen days with desquamation of great sheets of skin. The third man, who wore a loose gas-mask, had symptoms of eye pressure, cloudy vision and headache.

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#### 1d. BACTERIOLOGY AND PARASITOLOGY

(1d—1)

(1d—1)

On a Substitute for Nutrose in Culture Media.

E. Guldemeister, *Cntrbl. f. Bakteriol.*, 87:75, Jena, Sept. 1, 1921.

Ox-serum is diluted 1:10 with distilled water, and heated to 100° C. It remains fairly clear. When 0.02 to 0.03% sodium citrate is added, the serum remains perfectly clear after boiling. This serum is a perfect substitute for Barsiekow's nutrose solution, or for Leuch's potassium-albuminate serum.

Barsiekow's differential nutrient media, using ox-serum instead of nutrose, is made with 5-10 c.c. of serum and 95-100 c.c. of distilled water, sterilized for one hour in an autoclave. To this preparation is added 1 gm. of dextrose, lactose or mannite, previously dissolved in 5 c.c. of litmus solution over a water-bath. This is then mixed with the serum solution in the proportions noted in the foregoing, run into sterile test-tubes, and sterilized on three consecutive days for from fifteen to twenty minutes in a jet of steam.

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(1d—2)

(1d—2)

Influence of Sugars on Indol Production.

R. Appelmans, *Compt. rend. Soc. de biol.*, 85:725, Paris, Oct. 22, 1921.

Aërobic and anaërobic tests were made with *Bacillus coli*, *proteus vulgaris*, *Bacillus dysenteriae*, *Bacillus cholerae* and *Vibrio septicus*, on glucose, maltose, mannite, sucrose and lactose. Indol was determined by Salkowski's method after three or four days of incubation. Indol production is inhibited in proportion to the degree of fermentation, with gas production, of the sugar. Of 4 strains of *Bacillus coli*, all were negative with glucose and lactose; with maltose and mannite, 2 were negative, 2 feebly positive, with sucrose, all were positive. Of 3 strains of *proteus*, all were negative with glucose maltose and sucrose; with mannite and lactose, all positive. Of 2 strains of dysentery bacilli, both were negative with glucose; feebly positive with mannite, and positive with sucrose, maltose and lactose. One strain of cholera bacillus was positive with all the sugars. One strain septic vibrio was posi-

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tive for mannite, negative for the other sugars. The pseudodysentery bacillus is stated to be, when grown with glucose, an exception to the rule.

(1d-3)

**Growth of Fibroblasts and Hydrogen-Ion Concentration of the Medium.**

*Albert Fischer, J. Exper. Med., 34:447, Nov., 1921.*

The purpose of the experiments described in this paper was to determine the rôle played by the hydrogen-ion concentration of the medium with regard to the growth of a strain of fibroblasts (from embryonic chick heart) cultivated in vitro for a long time. The rate of growth was found to be markedly modified by slight changes in the hydrogen-ion concentration of the medium, optimum growth occurring at pH 7.4 to 7.8. Fibroblasts show more resistance to higher alkalinity than to higher acidity, growing for 4 to 6 generations in a medium having a reaction of pH 5.5, and for more than 10 generations in one of pH 8.5.

(1d-4)

(1d-4)

**Salt Effects in Bacterial Growth. I.**

*George E. Holm and James M. Sherman, J. Bacteriol., 6:511, Nov., 1921.*

The writers studied systematically salt effects, especially the qualitative and quantitative relationships of radicals, as related to bacterial growth, and they correlated these findings with other effects which have been noted in pure chemistry as well as in biology. References are made to the investigations in both fields. In this paper it is shown that salts do effect bacterial growth much in the same manner as they affect chemical reactions, coagulation, permeability, etc., and that this effect is modified by the hydrogen-ion concentration of the medium, and that such effects are probably great enough to be given consideration in bacterial culture. In connection with the experimental work, *Bacterium coli* was used. The medium used and the method of sterilizing and adjusting the pH is described in the text. The results are shown in tables and are briefly that the growth of *B. coli* in 1% peptone medium is accelerated or retarded by different salts in low molecular concentrations. The salt effects at various H-ion concentrations vary greatly. Those salts which accelerate seem to widen the H-ion range for optimum growth, while those which retard growth seem to narrow the limits for optimum activity. Cations and anions are both effective.

(1d-5)

(1d-5)

**Hydrogen-Ions, Titration and the Buffer Index of Bacteriological Media.**

*J. Howard Brown, J. Bacteriol., 6:555, Nov., 1921.*

In most laboratories, media are properly adjusted to certain hydrogen-ion concentrations, and the changes in reaction produced by the growth of organisms in these media are likewise determined in terms of hydrogen-ion concentrations. The titration of media is not to be regarded as a crude method of determining the reaction of media but a process which reveals facts not disclosed by a simple hydrogen-ion

determination. In literature, frequent references are made to the buffer content of media which indicates its importance. For many common purposes, a knowledge of the buffer content of media is quite as important as the hydrogen-ion concentration. Reference is made to the titration curves of bacteriological media published by Clark, Bovie, Clark and Lubs. These show that for the general purpose of determining the relative buffer values of media, hydrochloric acid may well be employed. The buffer content between stated limits of hydrogen-ion concentration is easily defined as the buffer index which is the sum of the reserve acidity and reserve alkalinity between those limits. A number of experiments were carried out to determine the buffer index, effect of cultures on the buffer index, influence of the reserve alkalinity and the amount of fermentable sugar on the final hydrogen-ion concentration and acid production by *Bacterium coli* and by a streptococcus. The values may be determined by the following methods: (1) The reserve acidity may be titrated with alkali from pH<sub>n</sub> to pH 8.0 and then using the same sample the buffer index may be titrated with acid from pH 8.0 to pH 5.0. The reserve alkalinity is calculated by subtracting the former from the latter. (2) The reserve alkalinity may be titrated with acid from pH<sub>n</sub> to pH 5.0 and then using the same sample, the buffer index may be titrated with alkali from pH to 8.0. The reserve acidity is calculated by subtracting the former from the latter. (3) The reserve acidity may be titrated with alkali from pH<sub>n</sub> to pH 8.0 in one sample and the reserve alkalinity titrated with acid from pH<sub>n</sub> to pH 5.0 in another sample, the buffer index then being calculated by addition to the other two values. The same results may be obtained by all three methods provided the dilution of the color of the medium and of the indicator is carefully controlled. The last method, a simple colorimeter method, is the simplest and can be performed in five minutes; the determination can be made by any laboratory helper who can make a titration or a hydrogen-ion determination and it should be recorded for each lot of medium made. In the appendix the method for the titration is described in detail.

(1d—6)

**On Decreasing the Exposure Necessary for the Gelatin Determination.**

*J. E. Rush and G. A. Palmer, J. Bacteriol., 6:571, Nov., 1921.*

The writers performed a series of experiments with several strains of bacteria isolated from water supply to test the desirability of a new and rapid method for determining the ability of organisms to liquefy gelatin. The present method is to subject the gelatin stab to a temperature of 20° C. for ten or fourteen days after inoculation and then note the results. The advised method, which is supposed to be just as efficient, is described as incubation at 37° C. for four days, followed by twenty-four hours' incubation at 20° C., after which the results are recorded. The latter method is obviously a time saver, liberates test-tubes from the incubators earlier and saves incubator space.

Inoculations of the same batch of gelatin were made in duplicate and controls from the same batch of media, prepared according to standard procedure, were used. A table shows the general results. No very definite statements can be made except that if it is desired to get the results by exposure to 20° C. for ten or fourteen days, these same

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results cannot be realized by exposure to 37° C. for four days and then to 20° C. for one day. A greater number of inoculations show liquefaction at 20° C. as time progresses. Also, certain cases show a definite increase in percentage liquefaction from the ten to the fourteen day period. The number of tubes which show liquefaction at fourteen days and none at ten days is, however, less than one-half of 1% of the total cultures examined. As a general thing, more cultures show liquefaction, or there is an increased amount of liquefaction, at 20° C., for fourteen days than by the new rapid method. In those inoculations in which a greater liquefaction by the more rapid method was noted, it was shown that in almost every case, total liquefaction occurred. The writers are unable to state the significance of this.

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(1d-7)

### Microscope Dark-Field Examinations and Errors in the Azimuth.

*F. W. Oelze, Cntrlbl. f. Bakteriol., etc. 87:76, Jena, Sept. 1, 1921.*

Many erroneous statements have appeared in the literature owing to incorrect observations on dark-field examination.

The most frequent source of error is a mistake in the azimuth. With the proper lighting the light emerges from the paraboloid condensor in the form of a hollow sphere. Its apex is the point where the rays cross one another, and that is where the specimen to be examined should be placed, so that the slide receives the light from all sides in an equally oblique manner. When the light fails to fall evenly on the plane mirror, the corresponding part of the surface of the condenser transmits no rays at all, and the specimen is not equally lighted in all its parts. As a result only certain portions of the specimen show up in the dark field; in the case of spirochetes only a tiny portion of their convolutions is illuminated and visible.

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(1d-8)

### Chart of the Families and Genera of the Bacteria.

*Harold Macy, J. Bacteriol., 6:575, Nov., 1921.*

An accompanying chart illustrates graphically the position of the orders, families, tribes and genera of the Schizomycetes. Macy makes no claim to the finality of this classification, but the chart may prove useful to bacteriologists who wish to have a convenient guide to the arrangement of the Schizomycetes under the proposed classification.

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(1d-9)

### Structure and Development of Bacteria.

*A. Kirchenstein, Compt. rend. Soc. de biol., 85:787, Paris, Oct. 29, 1921.*

The usual staining processes cause overstaining and prevent clear differentiation of the various parts of bacteria. Two methods are employed: (1) Carbolfuchsin is applied for from one-half to one second to the preparation, previously treated with a mordant, such as 5% chromic acid or 15% nitric acid. The culture, spread out on the slide, is rendered moist by the breath and is stained immediately after drying. This method is especially applicable to vibrios and pasteurella. (2) The

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(1d-9)

bacteria, first treated by a mordant, are stained as usual and differentiated. Alcoholic solutions of iodin or picric acid, of various concentrations, are employed. The duration of staining depends on the bacteria, but from one to ten seconds will usually prove satisfactory. The specimens are counterstained with methylene-blue. Granular particles occupy definite positions within the bacterial body. They stain more deeply than the plasma, and are probably composed of nuclear material. Most bacteria divide by amitosis. The process is more complicated in bacteria than in amebæ, the nuclear particles being connected by filaments. Triangular and spiral forms appear, and granules and filaments separate to complete the fission. Sporogenic bacteria divide similarly, but with somewhat of a mitotic process, essentially the analogue of that occurring in higher organisms. Nuclear substance of vegetative forms condenses in the spore. The "cytodes" of Haeckel do not occur in bacteria.

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Suggestions Concerning a Rational Basis for the Classification of the Anaërobic Bacteria. Studies in Pathogenic Anaërobes. IV.

Hilda Hempl Heller, *J. Bacteriol.*, 6:521, Nov., 1921.

An extensive study has been made of a carefully controlled series of certain groups of anaërobic strains secured from the following pathologic material: 23 strains from human wound infections, 32 from cases from so-called blackleg of cattle, 10 from cases of braxy and of the blackleg of sheep, and 15 from other animals. The collection included 30 odd strains of tetanus and other proteolytic organisms of various sorts. This collection has furnished so much material for investigation, and the information gained from them has so radically altered the writer's attitude towards the anaërobic group, that she presents the results of this investigation and proposes a new anaërobic classification. The value of the characters used for classification under former methods are discussed from the viewpoints of morphology of the vegetative cell, motility, spore formation, size of rod, arrangement of the bacilli in chains, morphology of the colonies, etc. It is demonstrated with what ease objections may be made to almost any morphologic character used for the division of the rods of higher metabolism, in case any physiologic character is allowed to enter into the classification. The more logical division of the bacterial rods is the physiologic one of susceptibility to free oxygen. If the anaërobic rods are placed in a common family on this basis, it may then be divided into 2 subfamilies on the basis of chemical action on carbohydrates and proteins. The divisions tribe and subtribe may well be left open for future organization. The old conception of species in the anaërobic group corresponds to the general systematists' conception of genera. Generic character may be based chiefly on qualitative behavior on ordinary media. Pathogenesis and general morphology may be used as auxiliary generic characters. Specific characters may be based on the sugar fermentations, on quantitative chemical action, on the morphology of colonies, to some extent on the morphology of individuals. A suggested classification of the anaërobic bacteria is given.

(1d-11)

(1d-11)

**The Pathogenicity of Bacillus Abortus and Bacillus Melitensis for Monkeys. Studies on the Genus Brucella Nov. Gen. III.**

*E. C. Fleischner, M. Vecki, E. B. Shaw and K. F. Meyer, J. Infect. Dis., 29:663, Dec., 1921.*

Bacillus abortus and Bacillus melitensis having already been shown to be closely related morphologically, biochemically, and serologically, the authors studied experimentally infected monkeys to determine whether the syndromes produced by the two organisms were similar. An intravenous inoculation of *B. abortus* caused agglutinins to develop fairly rapidly in the blood of monkeys. The animals may have an intermittent fever and lose weight. Organisms may be recovered from the spleen, lymph-nodes and liver after death, while even on the fourth day after the injection the blood-stream is sterile. By feeding glycerol-agar cultures of moderately virulent strains of *B. abortus* in large and repeated doses, definite infections were obtained in a fairly large percentage of monkeys. The duration of incubation, as judged by the appearance of serum agglutinins, is always prolonged. *B. abortus* can be isolated from the spleen and occasionally from other tissues. The repeated oral administration of massive doses of highly virulent *B. abortus* cultures causes a rapid development of specific agglutinins, but interruption of the feeding leads to a gradual diminution of the antibodies, probably on account of the disappearance of the bacteria from the tissues.

Milk of cows heavily contaminated with cultures of *B. abortus* of low virulence failed to cause infection when fed to monkeys for at least fifty-two days. The ingestion of cow's milk rich in agglutinins never led to an appearance of these substances in the serum of monkeys. Milk obtained from goats which had been experimentally infected with *B. abortus* of low virulence failed to produce infection in monkeys, even when fed for from twelve to forty-two days. One monkey was infected by repeated feeding of the milk of a goat infected by the injection into the udder of a very virulent strain of *B. abortus* of porcine origin. Serum agglutinins specific for the bacteria of the Brucella group are formed only in the presence of a definite infection. The ingestion of heat-killed, autolyzed abortion bacilli is antigenically ineffective in monkeys. Certain strains of *B. melitensis* which produce lesions in guinea-pigs resembling those of *B. abortus*, when injected into monkeys intravenously give rise to characteristic temperature and positive agglutination reactions, and the organisms are recoverable at the postmortem examination from various tissues. One atypical *melitensis* strain introduced via the alimentary canal was not always pyrogenic, but it stimulated agglutinins, and the ingested bacteria persisted for at least 57 days in the spleen and mesenteric lymph-nodes. The microscopic changes produced by *B. melitensis* or by severe *B. abortus* infection in the monkey resembled those of an early typhoid infection.

The conclusion is reached that virulent strains of *B. abortus* in sufficiently large dosage are pathogenic for monkeys, and that *B. melitensis* is far more invasive than *B. abortus*.

(1d—12)

**The Effect of Hydrogen-Ion Concentration on the Production of Carbon Dioxid by Bacillus Butyricus and Bacillus Subtilis.**

*Matilda Moldenhauer Brooks, J. Gen. Physiol., 4:177, Nov. 20, 1921.*

The method used has been described in a previous publication. The apparatus is a closed system, containing at each end 2 pyrex glass tubes in which are placed respectively the bacteria to be used and the indicator, the change in color of which measures the respired carbon dioxid which is forced through the system. A non-pathogenic acid-fast organism, *Bacillus butyricus*, was used; forty-eight hour cultures were grown on glycerin agar and incubated at 37° C. For comparison, the same experiments were also performed with *Bacillus subtilis*, a non-acid-fast organism, which had been planted upon agar-agar and incubated for eighteen hours at 37° C. previous to use. These organisms were then transferred to a 0.75% solution of dextrose in distilled water. For each experiment 2.5 c.c. of 0.75% dextrose solution (pH of 7.0) containing the organisms were used. The hydrogen-ion concentration of the solution was changed by adding drops of various concentrations of NaOH or H<sub>2</sub>SO<sub>4</sub>. The indicators used for determining the pH were thymol blue, bromphenol blue, methyl orange, methyl red, bromcresol purple, phenolsulfonephthalein, and phenolphthalein. Buffer solutions, made according to Sorensen's tables, were used as standards for comparison. Control experiments were performed with all the solutions in the absence of bacteria, and also with dead bacteria killed by boiling for one-half hour. The results plotted graphically show that the maximum rate of carbon dioxid production of *Bacillus butyricus* occurred at a pH value of 7.0; of *Bacillus subtilis* at pH 6.8. If the pH value were raised or lowered there was a progressive decrease in the rate of production of carbon dioxid. Spontaneous recovery followed the addition of alkali to either organism, while addition of acid was followed by recovery only upon addition of an equivalent amount of alkali, and was not complete except when the amount of acid was very small.

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(1d—13)

**The Capsules or Sheaths of *Bacillus Actinoides*.**

*Theobald Smith, J. Exper. Med., 34:593, Dec. 1, 1921.*

*Bacillus actinoides* produces capsules or sheaths only when grown upon coagulated serum. The capsules are present on the organisms in epithelial cells but absent in cellular exudates. They do not seem to be carriers of virulence. From two cases both sheathed and unsheathed forms have been isolated and continued indefinitely in pure culture. In freshly isolated organisms the capsules have optical characters closely resembling the myelins. In later cultures true fat droplets appear at the expense of the myelin-like material, and a gradual loss of the function of secreting the capsular substance occurs. The fact that some strains are found which do not form capsules should not cause confusion in identification if all the cultural characteristics are borne in mind.

(1d—13)

(1d—14)

**An Outbreak of Pneumonia in Dairy Cows Attributed to Bacillus Bovisepticus.**

*F. S. Jones and Ralph B. Little, J. Exper. Med., 34:541, Dec. 1, 1921.*

An outbreak of pneumonia occurred in a herd of cows and was believed to have started with the introduction into the herd of some recently purchased cattle. One of these was sick at the time, although the diagnosis of pneumonia was not made. The disease spread rapidly throughout the original herd, and to the calves which were kept at quite a distance, 20 cows and 2 calves being affected. Of 10 cases studied, 5 recovered. In the autopsies of those dying or killed, a diffuse pneumonia was found, and *Bacillus bovisepicus* was isolated from all involved portions of lung. The organism was not obtained from spleen nor kidney nor could it be found in blood cultures. Its low virulence, shown by inoculation experiments with rabbits and calves, was also indicated by the high percentage of recoveries among the affected cows.

(1d—15)

(1d—15)

**A Study of *Bacillus Bovisepticus*.**

*F. S. Jones, J. Exper. Med., 34:561, Dec. 1, 1921.*

Sixteen strains of *Bacillus bovisepicus* have been found to fall into 3 cultural and immunological groups. Specific agglutinating sera have been obtained from rabbits inoculated with cultures of the various groups. In no instance has cross agglutination occurred. The cultural characteristics of Group 1 differ widely from those of Groups 2 and 3, and it is suggested that perhaps the term *Pasteurella "bovisepicus"* should be applied to the members of Group 1.

(1d—16)

(1d—16)

**Some Characteristics of *Bacillus Chauvoei*.**

*Leonard W. Goss, Rhea E. Barbarin and A. W. Haines, J. Infect. Dis., 29:615, Dec., 1921.*

The authors describe the methods of preparation of mediums suitable for the growth of *Bacillus chauvoei*. *B. chauvoei* is discussed with regard to cultural and morphologic characteristics. A method for the rapid isolation of the organism from infected material is given. The failure of pure cultures of *B. chauvoei* to grow on 2% dextrose agar is, the authors believe, an important and much neglected criterion for judging the purity of such cultures. Cultures of *B. chauvoei* of high virulence for guinea-pigs are fatal to mice, though only in much larger doses than are necessary to kill guinea-pigs; and the amount of *B. chauvoei* culture required to kill a pigeon is many times greater than that required to kill a guinea-pig. Sheep are apparently somewhat refractory to natural infection with *B. chauvoei*, but can be successfully infected with large doses of virulent cultures. No strain of genuine *B. chauvoei* has been isolated from the tissues of sheep suspected of having died of blackleg. Kids may be fatally infected with pure cultures of the organism. Protection tests with anti-blackleg serum indicate a marked specific for *B. chauvoei*, and assist materially in its identification and its differentiation from *Vibrio septique*. It is possible that the agglutination reaction may be of use in the identification of this organism, but its study is still distinctly in the experimental stage.

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(1d—17)

**Induced Morphologic Variation in *Bacillus Coli*.**

*F. M. Scales, J. Infect. Dis.*, 29:591, Dec., 1921.

This investigation was made with strains of *B. coli*, *B. aerogenes*, and 4 unidentified organisms. The conclusions drawn are considered to apply only to *B. coli*, although they may be true of many non-spore-forming species.

The cultures employed, in general, were very stable, but one or two different strains showed some variation in morphology on all the special mediums, like egg starch agar, etc. When grown on standard beef agar, *B. coli* multiply almost entirely by fission, though some strains produce gonidia, the number of the latter being small, and varying with the strain. In one culture, gonidia were produced in abundance. The gonidia when liberated on standard mediums grow to rods, but on transplantation to a medium of high osmotic pressure, many rods die. The resultant growth is due either to the mass action of the organisms or to the presence of more resistant cells in the culture. The vitality of a culture is reduced by repeated transference to mediums of high solution pressure, and all degrees of sensitiveness to this environment have been found. Some rods and threads under special stimulus produce coccoidal bodies which arise from the growth of a nucleus within the parent cell. This type of growth was obtained on a medium of high solution pressure, i. e., 6% salt and 2.5% agar in the standard beef agar. These coccoidal growths may separate from the parent cell by the division characteristic of cells with either firm or soft walls. The division is accordingly sharply defined, as typically occurs in fission, or may be drawn out as in the case of sagittal segmentation. Both kinds of division are found in the same culture. The coccoidal cells may liberate small cells by sagittal segmentation. The large free coccoidal bodies become shadow forms and disintegrate, if left on the medium which produced them. A rod-like growth may originate within a mother cell and extend through the side wall of the parent. Odd-shaped cells are usually found in cultures grown on mediums of high solution pressure. Those cultures that readily respond morphologically to a change in environment show a tendency, on rich nitrogenous mediums like egg agar or egg starch agar, to form small coccoidal bodies at 37° C. and rods, larger than those on standard mediums, at 17° C. The great majority of the organisms tested in this work showed only slight variation under these conditions. The different morphologic types quickly revert to the normal laboratory type of *B. coli* when planted on a standard medium from a medium that has caused variation. In mediums of high solution pressure, all *B. coli* retained their physiologic activity though one or more functions of the strains were much suppressed. Gas formation was greatly retarded in all cultures and growth was delayed in Clark and Lubs' synthetic medium; the latter effect was very probably due to the absence of an organic buffer in this solution.

(1d—18)

**Biologic Modification of *Bacillus Coli* in Containing Phenol Media.**

*P. Fabry, Compt. rend. Soc. de biol.*, 85:884, Paris, Nov. 12, 1921.

When treated with gradually increasing quantities of phenol, the  
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(1d—18)

bacillus becomes accustomed to the latter, ceases to produce indol in its media, and preserves this new trait, so that, when regrown on media containing no phenol, the bacillus still does not produce indol. The bacillus can be made to live in a concentration of 0.2% phenol in bouillon. Once modified, so that indol is no longer produced, keeping the bacillus at laboratory temperature or growing in the peritoneum of guinea-pigs does not restore indol production. The other original staining and cultural characters are preserved; apparent changes in the microscopical appearance may be due to the polymorphic nature of the bacillus. Guinea-pigs in which the peritoneum is injected with 0.50 c.c. per 100 gm. body weight of a bouillon culture of the "modified" bacillus may die of peritonitis within forty-eight hours; the "modified" bacillus, when injected, may be recovered from the blood or peritoneal pus and form vigorous colonies on gelose. In one experiment, the bacillus (modified) was recovered after remaining for about ten days in the peritoneal cavity of a guinea-pig, where it had induced a slowly developing abscess; new cultures yielded all the usual characters of the unmodified bacillus, except the production of indol. The result has been uniformly obtained with bacilli of various origins.

(1d—19)

(1d—19)

**The Demonstration of Colon Bacilli in Water by Bulir's Test.**

*C. W. Jungeblut, Cntrlbl. f. Bakteriol., 87:63, Jena, Sept. 1, 1921.*

By Bulir's method, 1 kg. of chopped meat is macerated for twenty-four hours in 2 liters of water; the meat is then pressed and the juice is treated with 2.5% peptone, 5% sodium chlorid and 3% mannite. The whole is boiled over a gas flame, neutralized with potassium hydroxid, filtered and sterilized for two hours by steam. The water to be tested is then mixed with half its volume of the mannite-bouillon and 2% of a sterile solution of 0.1 gm. neutral-red in 100 c.c. water. This mixture is placed in a fermenting tube and kept at a temperature of 46° C. for a period of twenty-four hours. By this method in most cases, if *Bacillus coli* be present, bubbles of gas are formed in twenty-four or forty-eight hours.

In exceptional cases the evolution of gas fails even when *B. coli* is present, but when more sugar (or mannite) is added gas production ensues. No explanation of this remarkable property is offered. Water free from colon bacilli never gives the gas reaction. The decolorizing of the neutral-red occurs in too irregular a manner to be a reliable indicator, as it may occur in water free from colon bacilli. It is not proved that Bulir's method is any improvement on Eijkman's.

(1d—20)

(1d—20)

**New Method for the Bacteriologic Diagnosis of Diphtheria by Cultures on Enriched Media.**

*M. Pergola, Policlinico (Pract. Sect.), 28:1355, Rome, Oct. 10, 1921.*

The method includes cultivation and isolation of the bacteria. The liquid medium for cultivation consists of 50 c.c. of the normal blood of cattle, horses or sheep, 50 c.c. of an 0.8% solution of sodium chlorid, 0.02 gm. potassium tellurit and the yolk of one egg. This mixture, sterilized at 55° C., remains liquid. It is put in test-tubes in quantities of 5-7 c.c. and is ready for use.

The best solid media for isolation are (a) the same as the foregoing: (b) 50 c.c. ordinary agar, 50 c.c. of normal blood, 0.02 gm. potassium tellurit and the yolk of one egg. Medium a may be solidified by pouring it into flat dishes and heating it for about an hour to 85°-90°C. Medium b is prepared by adding the other ingredients to the melted agar and putting it in flat dishes.

The material suspected of being diphtheritic is emulsified in 2-3 c.c. of broth or sterile physiologic salt solution. A drop of this is put on the surface of the flat dishes of solid media and the rest is used for cultivation in the liquid media. After giving time for development the dishes are examined. If diphtheria colonies are found the test is ended. But if the result is negative, one or more dishes are sowed with a loop of material from the culture tubes which have been shaken to make the contents homogeneous, the dishes are put in the incubator again for another test. Positive results will not be obtained in less than twelve to fifteen hours from the sowing. After fifteen hours' incubation the diphtheria colonies are small, convex, elevated, shining, moist, ash-colored, but never black. The non-diphtheritic colonies are usually black, punctiform or large and flat. After twenty-four hours' growth the diphtheria colonies have increased in size and are a dull lead color which is more marked in the center and less so at the periphery; this makes them look as if they were surrounded by a clear ring. After twenty-four more hours, the diphtheria colonies may become a deep black. Neisser's method is recommended for staining the specimens. They should be treated with Lugol's solution, however, between the staining with methylene blue and that with vesuvin or chrysoidin.

(1d—21)

(1d—21)

**Metachromatic Granules in Diphtheria Bacilli.**

*Santo Racchiusa, Ann. d'Igiene, 31:545, Rome, Sept., 1921.*

By a study of the most characteristic properties of these granules, particularly metachromasia, it was sought to determine whether the substance of which they are composed act as other metachromatic bodies, such as the granules of mast-cells, mucin, amyloid, Reich's granules in Schwann's cells and the basometachromophil substance found by Alzheimer and others in nerve-cells and adventitious cells in pathologic cases. Of the metachromatic substances studied, mucin closely resembles polar granules. The polar granules may readily be demonstrated by the following methods: (1) Staining for from ten to twenty minutes with a 1:1,000 solution of thionin; differentiation in alcohol or in water acidulated with acetic acid; washing in distilled water. The granules are stained violet red and the bodies of the bacilli bright blue.

(2) Staining with dilute Giemsa stain for from ten to fifteen minutes; washing in water and differentiation in acetone or water acidulated with acetic acid. The granules are stained violet blue and the bodies of the bacilli a rose color.

(1d—22)

(1d—22)

**Biological Antagonism between Löffler's Bacillus and Friedlander's Pneumobacillus.**

*J. Gaté and G. Papacostas, Compt. rend. Soc. de biol., 85:859, Paris, Nov. 12, 1921.*

In observations on anginas where Löffler's and Friedlander's bacilli  
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were associated, the authors established three facts: Löffler's bacillus rapidly disappeared from the infected throats. The anginas were always benign. Löffler's bacillus gradually disappeared from mixed cultures. The latter fact was examined with various strains and culture media. Pneumobacilli invariably predominated over Löffler's bacilli which were killed off in thirty to forty days. They lived longest in the gelatinized serum; the Löffler bacilli became gradually longer, less granular and more homogeneous; they did not stain so well and resembled involution forms grown under unfavorable conditions. Pneumobacilli were planted on gelatinized serum, and the colonies which developed were removed with a platinum loop; Löffler's bacilli were then planted in their place. The latter grew slowly and poorly in such areas, but vigorously in other areas in the same tube. The pneumobacillus arrests the development of Löffler's bacillus, not by its presence alone, but by modifying the medium, possibly but not probably by abstracting nutritive substances; the action is probably due to the production of toxins which destroy the Löffler bacilli.

(1d—23)

(1d—23)

**The Atypical (Auto-Agglutinable) Bacillus of Shiga.**

C. Zoeller, *Compt. rend. Soc. de biol.*, 85:800, Paris, Nov. 5, 1921.

This form, auto-agglutinable in the usual culture media and physiologic serum, was prepared for study by emulsifying, in a 5:1,000 solution of sodium chlorid, the twenty-four-hour growth on gelose. It was agglutinated by anti-Shiga serum in dilutions of 100, 200, 500, 1,000 and 2,000, by anti-Flexner serum in dilutions of 100, 200 and 500. The precipitate appears in the form of a fine dust rather than of large flakes; it disappears on slight shaking. Increasing quantities of alexin were used in the study of the fixation reaction. Deviation of complement is the same for the typical and atypical forms. A rabbit vaccinated by an emulsion of typical bacilli killed by heat is vaccinated against the atypical bacillus, and vice versa. Attempts were made to transform the atypical to the typical form by means of several plantings in ordinary bouillon diluted with distilled water, in which the atypical form produces homogeneous clouding; but the atypical form remained auto-agglutinable when regrown in ordinary bouillon.

(1d—24)

(1d—24)

**A Study of the Gonococcus and Gonococcal Infections.**

M. W. Cook and D. D. Stafford, *J. Infect. Dis.*, 29:561, Dec., 1921.

This study was carried on for the purpose of devising improved methods for the diagnosis of gonorrhea and of determining whether strains of gonococci could be typed. It was found that gonococcus stock cultures grew satisfactorily for all routine work on testicular agar, and that chocolate blood testicular agar was a useful medium for increasing the vitality of a weekly growing culture. Environmental requirements of the organism included moisture of the atmosphere, but not a reduced oxygen tension.

Isolation of cultures was attempted from two types of cases (acute cases of anterior urethritis in men and chronic cases in women), and in the former cases was most successfully accomplished on chocolate blood testicular agar. No pure cultures of gonococci were isolated from chronic cases of gonorrhreal and endocervicitis, although single

colonies of organisms morphologically typical gonocci were obtained on plates of hydrocele testicular agar containing certain members of the tri-phenylmethane series of dyes as an inhibitor of contaminating organisms.

The alexin fixation test serves as an aid in diagnosis, but it should be still considered rather as confirmatory evidence than as an independent basis of diagnosis. It is of little value in early cases, as might be expected. A non-specific reaction was obtained on the intracutaneous injection of a preparation of gonococci. A like reaction was obtained in gonorrhreal patients on the injection of a preparation of meningococci. No typing of strains of gonococcus was obtained by means of the alexin fixation and agglutination reactions or by means of the method of absorption of agglutinins.

(1d—25)

(1d—25)

**Studies on Bacterial Nutrition. III. Plant Tissue as a Source of Growth Accessory Substances in the Cultivation of *Bacillus Influenzae*.**

*Theodor Thjötta and O. T. Avery, J. Exper. Med., 34:455, Nov., 1921.*

In preceding papers of this series, the authors have shown that the hemophilic bacilli require for growth two separate substances present in red blood-corpuscles, viz., (a) a vitamin-like substance readily extracted from the corpuscle, and (b) a so-called X substance. Experimental characteristics of these substances are described, including concentration necessary for growth, heat stability and absorption. These substances are found to occur in plant as well as animal tissue, which accounts for the fact that sterile raw potato may serve as a substitute for blood in the cultivation of *Bacillus influenzae*.

(1d—26)

(1d—26)

**The Significance of "Hemolytic Influenza Bacilli."**

*A. L. Bloomfield, Bull. Johns Hopkins Hosp., 32:378, Dec., 1921.*

In recent months a large percentage of the throats of healthy people have been found to contain plentiful cultures of a hemolytic Gram-negative hemophilic organism resembling the influenza bacillus. This organism has not previously been common. During November and December, 1920, it appeared in almost 100% of cultures, since then in about 50%. Such organisms as this must from time to time appear as temporary dwellers in the throats of large numbers of people, become colonized for a time, and finally die off, having failed to gain permanent adaptation to the new environment. No pathologic significance is attached to this particular bacillus.

(1d—27)

(1d—27)

**The Biological and the Serological Reactions of Influenza Bacilli Producing Meningitis.**

*T. M. Rivers and Lawrence A. Kohn, J. Exper. Med., 34:477, Nov., 1921.*

On account of the various opinions about the unity or multiplicity of strains of influenza bacilli, an intensive study was made of several strains from the group which had produced cases of meningitis, to standardize the cultural and serological work on influenza bacilli. The methods and details of the results of the work are given. Of 13 menin-

gitic strains studied, 11 were found to be alike culturally and fall into 2 groups by agglutinin-absorption tests; 2 strains stood alone. Four blood culture strains from pneumonia cases used as controls, differed from each other culturally and serologically. When these strains showed a relation culturally to members of the meningitic group, this was not confirmed by serological reactions. It is possible that certain group of influenza bacilli may produce influenzal meningitis.

(1d—28)

(1d—28)

**Notes on the Classification of Microorganisms. Classification of Bacterium of Hemorrhagic Septicemia.**

*S. Plasay and E. Fribram, Cntrlbl. f. Bakteriol., 87:1, Jena, Sept. 1, 1921.*

Among 20 strains of the bacillus of hemorrhagic septicemia of Kral's classification, 7 showed automatic movements in the hanging drop, while 13 were motionless. These strains were analyzed by the ferment-culture, and their power to decompose grape sugar, to coagulate milk, and to form indol was estimated. Rabbits were then given aqueous extracts of these strains to immunize them, and the immunity serums thus obtained were tested with their homologous and heterologous bacillary-extracts. It was thus immediately shown that the immunity serums contained a hemolytic thermostable immunizing element (ambococeptor), for sheep's blood. It was found that the immunizing serums only showed the phenomenon of complement combination with their homologous and not with heterologous extracts. From the morphologic and serologic experiments it was concluded that the cultures in question formed a continuation series, ranging from the non-fermenting, non-motile, non-flagellate strains under consideration, to the strains of bacteria with several flagella, which produce gas, sugar and indol from albumin, and also coagulate milk. During the experiments on controlling the coefficient of complement combination, no group reactions were recorded, and all these bacterial strains were relegated to a collective group as bacteria multoseptica.

This group, which falls into the classification of the bacteria hemorrhagica, presents the following characteristics: small, ovoid, bipolar, short bacilli which like the specific bacillus of hemorrhagic septicemia responded to the experimental inoculation of animals; its members have either no flagellum, or rarely, from 1-3. The number of individuals, in any culture, which are furnished with flagella is very small, and the flagella are extra-polar. The bacteria belonging to this group may be subdivided into three types: Type (1) No flagellum, do not produce gas or convert sugar, and do not form indol. Type (2) Solitary individuals of a culture bear 1, others 2-3 flagella; milk is not coagulated. Type (3) Solitary individuals of a culture bear 1, others 2 or 3, and quite a number 5 flagella. A few of the strains show gas-formation from grape-sugar, and the formation of indol, and coagulation of milk. One of the strains of bacillus pestis and one bacillus pseudo-pestis or pseudotuberculosis rodentium are not included in this group. These 4 groups are comprised in an order under the name *Bacillus hemorrhagica* or *bipolaria*. In a second order is relegated all the bacilli which when stained show 2 poles, which produce in experimental animals hemorrhagic pneumonia, but which grow sparingly if cultivated in albumin-free media. On this account they are classed in

a third order as albuminophilia from which are excluded the hemoglobinophilia, including the following groups: *B. influenzae*, *B. tussis convulsivæ*, *B. aegyptiacus*. This last mentioned group is so called because they can only be grown on nutrient media containing hemoglobin.

(1d—29)

**The Hemolytic Streptococci. I.**

*J. Martin Beattie, Brit. M. J., London, Nov. 12, 1921, p. 786.*

The high frequency of hemolytic streptococci in the human throat may explain the importance of these organisms as secondary invaders in a multitude of diseases. They may be present in normal throats, and under conditions not clearly understood, may become the actual causal agent of disease. It is significant that in various acute infections a common starting-point is the throat. An average of several observers in 4 common diseases (scarlet fever, measles, influenza, lobar pneumonia) shows the striking prevalence of hemolytic streptococci. From a review of the literature it seems that the streptococci present in the healthy throat are the important causal agent in the complications following infectious diseases; perhaps in respiratory complications the actual cause of the disease may so act on the respiratory mucous membrane as to render it susceptible to attack by these streptococci. Acute primary streptococcal infections are familiar. A case in point is related.

Streptococci differ considerably in morphologic characters, manner of growth, biologic activities and pathogenicity, so it is important to know what special type of organism is present in each case. More careful investigation will aid in determining whether the individual can be immunized to the action of streptococci. Numerous tests have been devised to determine whether streptococci should be grouped into several distinct species or as variants of 1 species; these are described.

From the experimental side it seems clear that the streptococci of human origin are not a unit, but that several types exist; these types can be differentiated by immunologic and other reactions, and the homologous serum can protect against infection. There is no real evidence of value that these homologous serums are of practical value in human disease, but a definite advance in this direction has been made. Most of the work has been done with hemolytic streptococci isolated from cases of bronchopneumonia.

(1d—30)

**Streptococcus Classification.**

*J. Henry Dible, Brit. M. J., London, Nov. 12, 1921, p. 789.*

The question of classification is involved, due to manifold schemes already proposed, and to the unsettled position of the question of mutation. Essentials for any useful classification in human bacteriology are: (1) simplicity; (2) sharpness of division; (3) a real meaning of any subdivisions so arrived at, relative to the significance of the organisms as disease-producing agents. Bacteriological classifications are often arbitrary divisions, aiming to separate organisms into groups convenient for practical purposes; but subclasses must not become too numerous for working purposes.

Holman's classification is discussed; here the organisms are divided into hemolytic and non-hemolytic groups; subgroups are based on sugar (Sec. 1—Page 106)

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reactions. Table I shows main classes. Table II shows how similarly the different subtypes of the hemolytic series are distributed over the various conditions in which they are found (feces, throat, blood, erysipelas and cellulitis, abscesses, middle-ear, mastoid, and cranial sinuses, etc.). Table III shows distribution of non-hemolytic streptococci drawn from the same source. Here again there is little difference in distribution of the various subgroups amongst themselves, in disease processes. One great difference is their site of distribution in the saprophytic state; the fecalis form is essentially an inhabitant of the feces, while all others occur relatively infrequently in the feces, but relatively frequently in the throat.

The author's classification is based on the fact that plotting the types against the properties, there is a definite and recurring tendency for the association of certain properties; each represents a center of variation around which an association of certain properties is grouped, which association may be taken to define a type. Work done with the organisms found in the feces shows the association is constant, and reduced to a mathematical formula, is a real association. Table IV shows what properties tend to go together. Table V gives the author's working scheme of classification, based on the above mentioned association.

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(1d-31)

**Studies on Acute Respiratory Infections. VIII. A Study of the Cultural and Serologic Relationship of Hemolytic Streptococci Isolated from Inflammatory Conditions of the Respiratory Tract.**

*Eugenia Valentine and Lucy Mishulow, J. Immunol., 6:301, Sept., 1921.*

This study was made to determine whether a dominant variety of hemolytic streptococcus could be isolated in cases of acute colds and influenza. While the streptococcus hemolyticus is frequently present in the throat, the hemolytic streptococci obtained from inflammations of the respiratory tract fell into many cultural groups and sub-groups. There were so few serologic similarities that the probability of a dominant strain seems remote. There was no correlation between the grouping and the type of the disease. These observations and the relative infrequency of hemolytic streptococci in inflammations of the respiratory tract apparently justify the conclusion that none of the strains were of primary etiologic importance. A series of tables clarifies the text and gives in detail the procedure and results of all tests.

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(1d-32)

(1d-32)

**Studies on Acute Respiratory Infections. IX. Differences in the Character of the Hemolytic Action of Streptococci and the Relative Value of Various Methods in Demonstrating These Differences.**

*Lucy Mishulow, J. Immunol., 6:329, Sept., 1921.*

The four methods of determining the differences in the hemolytic activity of streptococci are referred to and Lyall's tube hemolysis method and Brown's modification thereof are discussed in detail. Careful studies based on a series of experiments led Mishulow to conclude that the blood-agar plate, incubated for forty-eight hours, is a more reliable method than the tube method. (Sec. 1—Page 107)

liable method of determining the hemolytic action of streptococci because differences in hemolytic action can be observed which are not observable with the tube method. The differences in hemolysis are correlated with primary differences in the mechanism of hemolysis. The hemolytic action of the beta type is primarily due to a soluable extracellular hemolysin. The hemolytic activity of the alpha type is apparently due to the direct action of the cocci or to products liberated by autolysis. The plate method brings out these points and is therefore the more valid method on which to base a classification. A modification of the tube method, in which only the clarified broth is used for the test, is apparently an improvement on the regular method. However, it may fail to reveal hemolytic action in instances in which the plate method gives positive results. A tabulated comparison is made of the results with blood pour plates and the tube methods, and of the pH values and classification. Other tables demonstrate the hemolytic activity of extracts of streptococci, hemolysis tested on successive days of incubation at 37° C., and the resistances to heat which cause hemolysis and methehemoglobin production.

(1d—33)

**Isolation of Tetanus Bacilli from the Cerebrospinal Fluid.  
Report of a Case.**

*G. R. Lacy and Cecelia Murdock, J. Lab. & Clin. Med., 7:100,  
Nov., 1921.*

Interest attaches to this report because it is generally thought that in tetanus infections of human beings the bacillus remains localized near the point of inoculation and that the symptoms are due to toxins transported from that point. A patient developed tetanus symptoms twelve days after an operation for tuberculous orchitis and epididymitis. Four days later, the patient having had 80,000 units of tetanus antitoxin, a lumbar puncture was done and a sample of cerebrospinal fluid was examined. Smears from the sediment were negative. A guinea-pig inoculated with 0.5 c.c. of the centrifuged fluid developed no symptoms during two and one-half months. Deep dextrose-agar stick cultures, litmus, milk and cooked meat cultures were made and incubated at 37°. In forty-eight hours gas bubbles appeared in the agar stick culture. From this were obtained motile gram-positive bacilli. In seventy-two hours these bacilli contained the characteristic racket-shaped terminal spores. At this time the same type of bacillus was found in the meat medium. Anaërobic plates showed pure cultures of tetanus bacilli. Material obtained six days later from the operative scrotal wound was negative for tetanus bacilli. Failure may have been due to the missing of the tetanus area in making the swab or to the destruction, by that time, of the bacilli.

A guinea-pig injected with a saline suspension of the organisms from the dextrose-agar culture was found dead twenty hours later. A second guinea-pig inoculated with a smaller dose of the suspension developed spastic paralysis of the inoculated leg and tetanic convulsions when frightened. Injection of 2 c.c. of the heart's blood from this animal into another guinea-pig produced symptoms of toxic poisoning. Another guinea-pig, receiving the dextrose-agar material after boiling, did not develop symptoms. Two others were inoculated with the dextrose-agar cultures and antitetanic serum; one was unaffected, the

other developed delayed symptoms attributable to an insufficient dose of antitetanic serum.

The manner of operative infection is naturally a point of interest. It is suggested that the close proximity of the scrotal wound to the anus indicates a possibility of infection by the feces.

(1d-34)

(1d-34)

**A Method of Following Reaction Changes in Cultures of Acid-Fast Bacteria.**

*Esmond R. Long and Agatha L. Major, Am. Rev. Tuberc., 5:715, Nov., 1921.*

The Theobald Smith curve (1) furnishes highly suggestive leads on the metabolism of the tubercle bacillus. From a protein-glycerol mixture both alkali and acid are produced at rates more or less constant for a given strain. The chemistry of the change has not been definitely worked out. A method similar to that used by Frothingham is submitted, in which the change in reaction can be followed with a high degree of accuracy between the limits of pH 6.4 and 8.4 using phenolsulphonephthalein as indicator. Four 1 in. test tubes, each containing 10 c.c. of glycerolpeptone broth or any other liquid medium, neutral in reaction (pH 7.0) plus 0.001% phenolsulphonephthalein, are inoculated with plaques of tubercle bacilli, approximately 0.75 cm. in diameter, sealed with tinfoil and incubated at 37.5° C. Once a week the tubes are taken out and the color compared with standards. The Dernby and Avery (6) comparator was used, placing a tube of broth back of the standard when determining broth reactions, to compensate for the color of the medium. Care must be taken that the plaque remains floating. The reactions of the 4 tubes are averaged in plotting the curve. Following is a summary of results: *Saprophytes*: On glycerol-peptone broth the grass bacillus caused a slight acidity, the timothy bacillus a distinct alkalinity, and the smegma bacillus little change, in spite of good growth. On alanin the grass bacillus caused a distinct acidity, the timothy bacillus a distinct alkalinity and the smegma bacillus little change. It will be noted that these results are about the same. This is to be expected in view of the fact that peptone consists almost entirely of polymerized amino-acids like alanin. The glycerol, highly necessary as it is for tubercle bacilli, probably plays little part here, as these organisms thrive on peptone alone. On propionamid, which differs from alanin in the location of its amino group, all organisms caused a marked alkalinity. *Tubercle Bacilli*: H37 on glycerol gave the curve generally considered to be characteristic of human type bacillus, a primary alkalinity followed by progressive acidity. B1 also gave the curve said to be characteristic for the bovine type, an initially increasing alkalinity, which later decreased, but not to the point of neutrality. H104 culture became alkaline and remained so for some months. No change was noted in any of these cultures after that time. The curve of H104 was thus not of the classic human type, but one of the numerous exceptions.

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**Chemical Problems in the Bacteriology of the Tubercle Bacillus.**

*Esmond R. Long, Am. Rev. Tuberc., 5:705, Nov., 1921.*

With human, bovine and avian tubercle bacilli, frog, turtle and fish  
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bacilli, leprosy bacilli, smegma bacilli and several strains of grass and mist bacilli, it was found that nitrogen is readily abstracted from the amino-acids alanin, leucin and histidin, and these may serve successfully as the sole source of nitrogen. One conspicuous exception lies in the inability of the 2 avian strains to utilize alanin; they, however, deaminize leucin readily. The tubercle bacillus is able to thrive with alanin, leucin and histidin as sources of nitrogen, but not with tryptophan or phenylalanin. Tubercle bacilli are unable to synthesize all the carbonaceous portion of their body substance from the material left after the abstraction of nitrogen, they need something else, preferably glycerol. Propionamid is readily deaminized by all organisms of the group, and ammonia is a sufficient source of nitrogen for all; creatinin is used for nitrogen fairly readily by smegma and grass bacilli, somewhat sparingly by frog, fish and turtle bacilli, less readily still by leprosy bacilli, and by tubercle bacilli not at all. Urea is used readily by all forms except tubercle bacilli and turtle and fish bacilli. The ready use by leprosy bacilli is noteworthy. Following the addition of certain market preparations of water soluble (yeast) vitamin, no growth increase with tubercle bacilli or other acid-fast organisms was noted, which could not be attributed to the presence of certain useful amino-acids in the absence of any vitamin constituency. On the other hand, certain amino acids are useful per se.

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(1d—36)

**A New Process for the Enrichment of Tuberculosis Bacillus with an Emulsion of Mastic.**

*R. Pfeiffer, and W. Robitschek, Cntrlbl. f. Bakteriol., 87:27, Jena, Sept. 1, 1921.*

Mastic emulsion is prepared in the following manner: The mother-liquor is a maceration of 100 gm. mastic in 900 gm. alcohol, made up to 1 liter. To prepare the emulsion for the test, 0.5 c.c. of this tincture is taken, diluted to 5 c.c. with absolute alcohol, and then emulsified by blowing through the pipette under 20 c.c. distilled water. The practical application is then conducted as follows: 50 c.c. of the sputum to be examined is first triturated with 150 c.c. distilled water, placed in an Erlenmeyer flask with continual stirring and shaking on the water-bath and warmed until almost complete homogeneity is reached (about half an hour).

From this sputum mixture about 8 c.c. is taken and placed in a centrifuge tube, with 2 c.c. of the above-described mastic emulsion, well mixed; it is then incubated for twenty-four hours. It is then centrifuged. Three preparations are made, one from the upper stratum, at the lowest point of the clear layer, one from the middle, and the third from the bottom of the sediment. Better results from this process have been obtained than with any hitherto employed.

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(1d—37)

**Detection of the Tuberclle Bacillus in Pathologic Products through Processes of Homogenization.**

*A. Bernard, J. d. sc. méd. de Lille, 39:377, 397, Nov. 27, Dec. 4, 1921.*

The general principles of homogenization methods are outlined. The sputum is rendered more fluid and homogeneous by various physical  
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and chemical means or by the use of diastases. In order to collect the bacilli together other liquids are added in order to increase or decrease the specific gravity of the fluid in comparison with that of the bacilli, which varies between 1.000 and 1.080. In the first case the bacilli float in the superficial layers of the liquid while in the latter they settle to the bottom of the container.

Homogenization is accomplished by adding 8 or 10 parts of filtered and sterilized ox-bile to 1 part of sputum. After shaking vigorously 2 drops of tincture of iodin per c.c. are added, the mixture is boiled for a few minutes or left in an incubator for eighteen hours, after which liquefaction is complete. To the cooled solution are added one-third of its volume of saturated salt solution, and 2 or 3 c.c. of ether. The mixture is centrifugalized at a speed of 1,500 revolutions per minute for five minutes. The bacilli will be found in the upper part of the tube between the bile and the ether. Of 73 negative examinations of sputum by the direct method 35% proved positive after homogenization. The method is recommended for its rapidity and simplicity, the small quantity of solvent used and the intact condition of the bacilli.

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(1d-38)

**Homogenization of Tuberculous Sputum by Spontaneous Autodigestion.**

*M. Favre and J. Devuns, Compt. rend. Soc. de biol., 85:858, Paris, Nov. 12, 1921.*

Although it does not concentrate all bacilli present, spontaneous autodigestion facilitates the search for tubercle bacilli by increasing their concentration considerably. Left alone at laboratory temperature for four or five days, the sputum separates into two layers; the upper is serous, the lower, one-third to one-half the original volume, is greenish and contains all of the bacteria. Specimens may be allowed to stand for ten to fifteen days; at 37° C. or in summer, the time may be shortened, but the higher temperature causes a growth of bacteria other than those of tuberculosis, which interfere with the examination. The results are more exact than those obtained by examining particles of pus. The method is especially useful for repeated examinations in the same case or for large numbers of smears.

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(1d-39)

**Comparative Experiments on the Demonstration of the Tubercle Bacillus by the Various Color-Tests of Ziehl-Neelsen, Gasis-Teleman, Kronberger, Unna-Pappenheim and Kronrich.**

*W. Bernblum, Cntrlbl. f. Bakteriol., 87:23, Jena, Sept. 1, 1921.*

Sputum was stained by each of the methods named in the title, and in the individual specimens, the tubercle bacilli which had taken the stain were counted. It was found that in those specimens stained by the Ziehl-Neelsen or Kronrich method, by far the greater number of the acid-fast bacilli were plainly visible.

The Ziehl-Neelsen procedure is as follows: The slide should be stained with undiluted carbolfuchsin over a flame until steaming, decolorized with 3% hydrochloric acid in alcohol, rinsed in water and counterstained with 1% aqueous methylene-blue.

Kronrich's method includes (1) staining for from one-half to two minutes in hot carbolfuchsin; (2) washing thoroughly; (3) decolor-  
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izing with a 10% sodium sulphite solution and rinsing in water, and (4) steaming for from fifteen to thirty minutes in aqueous malachite-green solution (1 part saturated malachite-green solution in 2 parts water).

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**Cultivation of Rickettsia-Like Bodies in Typhus Fever.**

*Leo Loewe, Saul Kitter and George Baehr, J.A.M.A., 77:1967, Dec. 17, 1921.*

The writers have succeeded in recovering from the blood of typhus fever patients minute bodies which are, morphologically and tinctorially, similar to Rickettsia prowazekii, which is the name that has been given to minute bodies found in the stomach wall of typhus-infected lice. Similar studies were carried out on a strain of typhus virus originally obtained in Poland and kept alive by numerous successive passages through animals. The organisms were recovered from the blood, brain and kidneys of guinea-pigs in which the disease had been produced by a previous intraperitoneal inoculation of culture material.

The bodies cultured by these methods differ in morphology and in cultural characteristics from the bacillus of Plotz, but what rôle the Plotz bacillus plays in the disease and what relationship, if any, it bears to these bodies is still to be ascertained. This study seems especially desirable in view of the fact that Olitsky, Denzer and Husk cultivated the Plotz bacillus from typhus-infected lice.

No decision is as yet permissible as to the identity of the bodies with Rickettsia prowazekii. Morphologically and tinctorially they are probably indistinguishable. The best evidence is the presence of these bodies intracellular in the walls of vessels in the brain and other tissues, sites in which rickettsia are found, and their increase in numbers at these sites when the tissues are incubated in culture mediums.

Whether the bodies are of bacterial or of protozoan nature has not yet been decided, but it is an unusual type of organism.

(1d—41)

**Experimental Studies on the Etiology of Typhus Fever. I. Concurrent Infections during the Course of Experimental Typhus Fever in Guinea-Pigs.**

*Peter K. Olitsky, J. Exper. Med., 34:525, Dec. 1, 1921.*

Three strains of typhus fever virus were used, two human and one louse strain. They were shown to be identical by cross-immunity tests. The strains were transmitted through a series of guinea-pigs by intraperitoneal injections of blood obtained by cardiac puncture from previously infected animals. Blood and spleen cultures were made from guinea-pigs during the incubation period and during the first four days of fever. The organisms thus obtained were *Bacillus typhi exanthematici*, an anaërobic streptococcus, *Staphylococcus aureus*, a *Gaertner* type bacillus, an aerobic diphtheroid, *Bacillus proteus*, *Bacillus welchii*, and an anaërobic gram-positive diplobacillus. The total number of positive cultures was 24, or in 41% of the 58 guinea-pigs. The organism most frequently found was the *B. typhi exanthematici*, obtained from 3 spleen and 5 blood cultures.

However, in view of the fact that the virus could be obtained during the incubation period of the disease without any admixture of cul-  
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tivable organisms, it is believed that these bacteria are secondary invaders and are unrelated to the true virus of typhus fever. The less common bacteria found were not pathogenic for guinea-pigs while the commoner forms produce conditions quite distinct from typhus fever.

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**Recent Studies of the Pathogenesis of Filtrable Virus.**

*A. Salvat, Rev. españ. de med. y cir., 4:581, Barcelona, Oct., 1921.*

Recent literature on encephalitis lethargica is reviewed. There is striking analogy between the 3 viruses of encephalitis lethargica, epidemic poliomyelitis and rabies. Herpes, except zoster, is due to a filtrable virus. Typhus and yellow fever are 2 other examples, and veterinary medicine supplies instances, such as the virus of hog cholera and bovine peripneumonia.

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**Elemental Corpuscles of Some of the Filtrable Viruses.**

*Rodríguez Méndez, Gac. médica catalana, 59:168, Barcelona, Sept. 30, 1921.*

Not all of the virulent principles of the filtrable viruses are now invisible. Microscopic investigation now reveals elements in many of these viruses which without doubt are the infective agents. In the pleuropneumonia of cattle, the vaccinia of cows, the epithelioma contagiosa of birds, in trachoma and molluscum contagiosum, elemental corpuscles have been observed by staining with Loeffler's or Giemsa's stains, methylene blue or preferably with arsenical nitrate of silver. The latter increases the dimensions of the corpuscles by chemical action and so renders them more visible.

Clear images of the elemental corpuscles of molluscum contagiosum, *Strongyloplasma hominis*, with a clear background, are obtained by use of the silver stain either in filtered or unfiltered virus. In the filtrate of vaccine lymph are seen very clear granular images of a black color and either isolated or in groups of two or three. Investigation of rabies virus was begun by using a lightly centrifuged emulsion of the medulla oblongata of a rabid rabbit; the images were confused by the presence of extraneous bodies but after filtration a few granular corpuscles of 0.3-0.4 microns, black, and single or in pairs were seen. After centrifuging for two hours the corpuscles showed a tendency to form in groups of two or three which made their recognition easier. After prolonged study it was decided that these were elemental corpuscles similar to those described as chlamydozoa. Future study is required to show what diagnostic value they have in rabies. Unless considerable care is used, error may occur from the presence of albuminolipoid bodies, which Lipschütz calls "cistoconos" in the filtered virus; this can be avoided by prolonged washing in distilled water and drying in the air. These bodies can be differentiated from elemental corpuscles by their smaller size, bad staining qualities, their great number in uniform distribution and their property of refracting light.

Bradford has isolated the elemental corpuscles of poliomyelitis, encephalitis lethargica, trench fever, influenza, nephritis, and rabies and has established the etiology of scarlet fever, measles, typhus fever, variola and parotitis.

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**Encephalitic Virus in the Cerebrospinal Fluid.**

*C. Kling, H. Davide and F. Liljenquist, Compt. rend. soc. de biol., 85:823, Paris, Nov. 5, 1921.*

Experimental encephalitis lethargica can be transmitted in series, proving that the cerebral lesions are caused by a virus living in the central nervous system. The responsible agent is resistant to glycerin, is filtrable, invisible, and cannot be cultivated. Thus far, attempts to communicate the disease by means of the cerebrospinal fluid have not succeeded. From a case, resulting in recovery, in a woman 40 years of age, the authors obtained cerebrospinal fluid by lumbar puncture; cultures on gelose were negative. The fluid was inoculated into 4 rabbits. The animals appeared to be healthy thirty-eight days after inoculation, and were then killed and examined. Macroscopically, there were no cerebral or other lesions; aerobic and anaerobic cultures remained sterile; bacteria were absent from the smears. A microscopical examination of 2 brains was negative; 2 other brains presented lesions typical of encephalitis lethargica. It is surprising that lesions so pronounced as these failed to produce symptoms. Other experiments by the authors indicate that encephalitic lesions in rabbits may exist without symptoms. To test the virulence in the animals with lesions, 5 rabbits were inoculated from the brains of the 2 rabbits affected. No symptoms appeared. Twenty-five days after inoculation, 2 of the 5 were killed; both brains presented typical lesions. The virus must therefore have been active. Inoculation of human cerebrospinal fluid into rabbits is a method of diagnosis.

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**Pure Culture of Small-Pox Virus.**

*W. Fornet, Cntrlbl. f. Bakteriol., 87:36, Jena, Sept. 1, 1921.*

Raw lymph was freed from contaminating bacteria by passing the ether vapor through it, and by means of a special apparatus devised by the author, this purification was effected in from 5 to 10 minutes. If resistant germs are present, the passage of the ether vapor is continued somewhat longer. Other sterilizing agents may be used instead of ether, such as petroleum ether, benzol, carbon disulphid and trichlorethyl.

The purified lymph serves as a base for the experiments in pure culture. Grape-sugar serum bouillon is used as a culture medium under anaerobic conditions. After seven to ten days of incubation, the increase in virus is recognizable not only by experiment on the living animal, and by the method described by Paschen (using Löffler's fixing solution and carbolfuchsin), but also as follows: 1% grape-sugar bouillon with indigo added to it is put in capillary tubes as a culture medium. The medium is at first blue, but after several days incubation at 30° C. it gradually becomes green and finally canary yellow.

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**The Diagnosis of Variola by Inoculation of the Cornea of the Rabbit.**

*W. H. Hoffmann, Med. Rec., 100:936, Nov. 26, 1921.*

A small quantity of the secretion from a suspicious pustule is removed by a small knife or needle, previously sterilized, and placed on a sterilized slide, cleansed by alcohol. The slide is put in a Petri dish  
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and allowed to remain for some time. The dried secretion may be used for the test. It has only to be moistened at the moment of inoculation of the animal with Ringer's solution or a few drops of a 50% glycerin solution in water. The rabbit may be of any kind or size. With a small sharp steel needle, previously sterilized by flame, there are made from 3-5 superficial horizontal incisions across the epithelium of the cornea of the eye, and as many in the vertical direction, crossing the first group of lines. A quantity of the secretion to be tested is then placed on the cornea with a small blunt properly sterilized instrument, and thoroughly distributed by a closing movement of the eyelid. The inoculated animal is then placed in a cage and treated as a highly contagious case. If no specific variola infection of the cornea has taken place, the small traumatic lesion will be healed in twenty-four hours; and after forty-eight hours the cornea will appear absolutely clear and without irritation. If, however, the eye has become infected with variola virus, there will appear on the cornea from thirty-six to forty-eight hours after injection, certain lesions which are visible to the naked eye, but are much clearer under a low power lens. There is proliferation at the site of the inoculation, which progresses rapidly, extends to the surrounding tissues, and is followed by epithelial desquamation in the central parts. The rabbit may be killed and sections made according to the method used in ophthalmologic work. Such sections show under low power the characteristic histologic lesions of epitheliosis variolica of the cornea of the rabbit. At higher power Guarnieri bodies may be seen in the swollen epithelial cells of the cornea. Though the histologic examination is not absolutely necessary for diagnosis of variola, this method tends to confirm and to increase the confidence of the scientific worker in Paul's proceeding for diagnosis of this disease.

(1d—47)

**Experimental Pulmonary Mycosis in Guinea-Pigs.**

*Ralph W. Mendelson, J. Trop. Med. & Hyg., 24:292, London, Nov. 15, 1921.*

In order to test out the pathogenicity of some of the moulds from a large collection recovered from human cases of pulmonary mycosis, Mendelson selected one at random and used it to produce an experimental pulmonary mycosis in guinea-pigs. The monilia grew abundantly on ordinary glucose agar. The guinea-pigs infected were carefully observed for one month; at the end of that time they were killed and examined for lesions. During the month they showed no signs of active illness. Illustrations show the presence of tumor-like masses resembling the condition found in tuberculosis of the lung. On examination, these masses proved to be mycotic tumors made up of connective tissue, a condition similar to some human cases. These tumors are nourished seemingly from the surrounding healthy tissues and do not tend to break down. Microscopic examination showed solidified areas due to air vesicles filled with red blood cells or with fibrin. General leukocytic infiltration was slight. Dilations of the capillaries and hyaline thickening of the vesicular walls occurred in some areas making the spaces smaller. The capsule of the enlarged peribronchial lymph-nodes were greatly thickened by a new and cellular fibrous tissue, the interior being a mass of polynuclear leukocytes which only partly fill

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the space inclosed by the capsule. The mycelial element of the original monilia could not be demonstrated but conidia were present in many of these areas. The control pigs were negative. Diagnosis was bilateral mycotic bronchopneumonia, subacute bronchitis and peribronchial lymphadenitis.

From a public health point of view, pulmonary mycosis is of great importance and only differs from tuberculosis in degree. It is contracted in the same way with the exception of infection by milk; it is incapacitating but preventable. It should receive the same careful attention other pulmonary infections do.

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(1d—48)

**Supplementary Note on a Case of Bronchomoniliasis in a Native of the Gold Coast.**

*J. W. S. Macfie and A. Ingram, Ann. Trop. Med. & Parasitol., 25:285, Liverpool, Sept. 30, 1921.*

In a previous paper, a fungus of the genus Monilia isolated from a case of bronchomoniliasis was described. It was then impossible to determine whether it was *Monilia nivea*, or a different species because the action on raffinose was undetermined. It has since been found that this organism does not produce acid or gas in raffinose. It cannot be regarded as *M. nivea* and the writers propose the name of *Monilia accraensis*. They have recently isolated the same organism from the sputum of another native patient at Accra; when tested immediately after isolation, it was found to produce neither acid or gas in raffinose.

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(1d—49)

**A Fungus of the Genus Nocardia Cultivated from Heart Blood.**

*J. W. S. Macfie and A. Ingram, Ann. Trop. Med. & Parasitol., 25:283, Liverpool, Sept. 30, 1921.*

The fungus found was cultivated from blood withdrawn from the heart at the autopsy of a patient who died of an obscure complaint. He was a native, aged 25 years old, regarded as suffering from encephalitis lethargica. The findings at the autopsy are given. The organism from the heart grew well on blood agar and nasgar at 37° C. and at the laboratory temperature, 26° C., producing a somewhat slowly spreading growth which was very firmly adherent to the medium. Colonies were smooth and dome-shaped, but finally became puckered and opaque in the middle and radially striated and semi-transparent at the periphery. Microscopic examination showed the growth to be composed of freely branching non-septate hyphæ about 1 micron or less in diameter. The hyphæ were more or less fragmented in older cultures. The ends of some of the filaments were slightly thickened and club-shaped. There was no growth on glucose or maltose agar nor on gelatin, ordinary broth or peptone water. The organism was Gram-positive but not acid-fast. Its qualitative biochemical reactions were tested, and no change was produced in any of the following: arabinose, rhamnose, galactose, glucose, levulose, mannose, lactose, maltose, saccharose, man-nitol, litmus milk, etc. This organism the writers named *Nocardia cruoris*. It had all the characters of a fungus of the genus *Nocardia*, but does not correspond with any of the numerous species already described.

(1d—50)

**Staining of Spirochetes in Smear Preparations.**

*Luigi Pais, Gazz. d. osp., 42:899, Milan, Sept. 22, 1921.*

The latest methods for staining spirochetes were studied with a view to determine which one of the innumerable procedures in vogue had the greatest practical use for rapidity, simplicity and excellence of results. The following methods were tried extensively: (1) The rapid method of Preis-Giemsa, by flushing the smear on a slide with freshly prepared Giemsa's stain, heating to steaming (but not boiling), pouring off excess fluid, adding it again and repeating the process 3 or 5 times, then washing and drying. The spirochetes stain a deep pink. The preparation is ready in five minutes. (2) Burri's negative method, by mixing a drop of suspected serum with an equal amount of China ink, quickly and thoroughly, smearing thinly with another slide (like a blood smear), drying in a current of air without heating. The spirochetes appear as clear as spirals, occasionally even the flagellæ being visible. (3) The Fontana-Tribondeau method, of applying to the dried smear a few drops of Ruge's solution (acetic acid crystals, 1 part; formalin 40%, 2 parts; distilled water to make 100 parts) repeatedly in the course of a minute, washing, fixing with a solution containing 1% phenol and 5% tannin, gently warming, washing off excess tannin, impregnating with a 0.25% ammoniacal solution of silver nitrate, gently warming until the preparation becomes chestnut brown, washing and drying. The spirochetes appear black against a yellow background. (4) Becker's method of applying to the dried smear a few drops of Ruge's solution repeatedly in the course of a minute, washing quickly, fixing by gently heating with a 10% tannin solution, washing, restaining with Ziehl's fuchsin for half a minute, washing, drying and mounting in Canada balsam. Spirocheta pallida is stained bright red against a faintly pink background; other spirochetes (*S. refringens*, *S. vincentii*, *S. balantitis*, *S. buccalis*, *S. dentium*) appear in various distinctive shades of red, much darker.

The Preis-Giemsa method appeared to greatest advantage for rapidity, ease of procedure and fine visibility of the preparation. Drawbacks are the easy formation of precipitates which obscure the field, and the cost of the reagents. The negative method of Burri is much simpler, but the reagent is difficult to prepare and costly. From a practical standpoint the method of Fontana-Tribondeau is easily the most preferable: the reagents are cheap and readily obtainable, the various spirochetes, especially *S. pallida*, are very well shown, and owing to their dark color the preparations lend themselves readily to microphotography. But the specimens do not keep long, becoming decolorized from exposure and from contact with cedar oil or Canada balsam. Becker's method has all the advantages of the Fontana-Tribondeau, and in addition the specimens keep indefinitely, the various species of spirochetes can readily be differentiated, even their detailed structure being clearly revealed, and the staining is clear and even. This last method may also be employed in staining smears from organs of congenital syphilites, and from gangrenous tissue previously fixed in formalin; to demonstrate *S. pallida* in condyloma acuminata, and *Strongyloplasma hominis* in *molluscum contagiosum*; even to show the presence of the bacillus

(1d—50)

of Ducrey. It has also given excellent preparations of Vincent's spirillum. Becker's method is therefore apparently the simplest and most satisfactory.

(1d—51)

**Spirochetes of the Buccal and Tracheobronchial Regions.**

*H. Viole, Compt. rend. Soc. de biol., 85:695, Paris, Oct. 22, 1921.*

Spirochetes occur in the dento-alveolar portion of the buccal region. They may be abundant in pyorrhea, Vincent's angina, Castellani's bronchopulmonary spirochetosis and hemorrhagic bronchitis. Hitherto they have not been found in the mouths of breast-fed and artificially-fed infants, nor in the Paris milk supply. Abundant in the child and adult, they are probably derived from the soil. They occur in great variety in Paris mud and sewage but rapidly disappear from this medium, which is alkaline and rich in ammonia and hostile microorganisms. But they survive for a long time in activated sludge, which is practically neutral and rich in nitrates oxidized from ammonia, and from which 90% of other microorganisms disappear by oxidation and agglutination; in old laboratory sludge they survive for more than a month and in continually activated sludge for more than two years. They prefer soil which is richly organic, neutral or faintly alkaline and very moist and aerated. Transfer to man probably occurs through insufficiently cleansed fruit and vegetables. The poor hygiene of certain Oriental and African peoples permits buccal and bronchopulmonary spirochetosis. The mouth being favorable, the organism may remain there indefinitely and cause angina, tracheobronchitis, and other diseases. Prophylaxis is easy, but treatment difficult, even with arsenobenzol or bismuth.

(1d—52)

**Morphology of Spirochæta Pallida.**

*J. Saphier, Arch. f. Dermat. u. Syph., 136:59, Berlin, Sept. 12, 1921.*

Important conclusions are drawn in this report from the morphologic appearance of Spirochæta pallida. Meirowsky devoted much study to changes in form of the spirochete, and drew the following conclusions: (1) The findings are the same in spirochetes obtained from cultures and those obtained direct from the tissues. (2) Nuclei, blepharoplasts or the vibrating membrane cannot be demonstrated in *S. pallida*, but only a deeper staining of certain convolutions. (3) Flagella (terminal fibers) are said to appear on transverse segmentation, and are due to the uncoiling of the spirochete to form a straight thread. (4) Transverse segmentation certainly does occur. (5) There is probably also longitudinal segmentation, indicated by the frequent appearance of divided gemmules. (6) The spirochete multiplies by gemmation (spore formation), chromophil substance collecting in thick masses in the body of the spirochete before gemmation, as it does in tubercle and leprosy bacilli. The gemmules are young, or perhaps permanent, forms of the spirochetes. (7) This variety of germination (by spore formation) and the absence of the characteristic structure of the protozoa indicate that *S. pallida* belongs in the class of bacteria, and probably to the higher forms of fungi.

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Saphier could not confirm Meirowsky's findings in sections stained by Levaditi's method as the spirochete remained quite plump. But this discrepancy was overcome to some extent at least by Jahnel's method which Springer also used in examining the brain of a paralytic. Saphier examined sections of the skin of a fully developed congenital syphilitic fetus, which he had prepared in 1920, and he almost entirely confirmed the observations of Meirowsky and Springer. He believes that the structures observed by Meirowsky and Springer were reproductive forms.

As to classification, Saphier agrees with Doflein that in "their structure, their manner of reproduction and their general life-history, the spirochetes have much more in common with bacteria than with protozoa."

(1d-53)

**On Some Nematode Parasites of the Camel in India.**

*C. L. Boulenger, Parasitology, 13:311, London, Nov., 1921.*

A complete description of 2 species of strongylid worms, *Haemonchus longistipes* and *Nematodirus spathiger*, is presented. This is apparently the first complete description of the two parasites. Hitherto there has been some confusion between the types of the various species. By the measurements given in the text *H. longistipes* proved to be somewhat larger than the type species. The male may be distinguished from those of *M. contortus* by the character of the posterior ray of the bursa, by the size of the coacal lip and by the length of the spicules, as well as by the position of the barbs at the posterior extremities of these structures. In the female the linguiform process over the vulva is lacking in fully developed specimens. They may be recognized by the measurements of the eggs, which are smaller than those of the type species. The measurements and structure of *N. spathiger* were found to agree with those of *N. nauritanicus*, given by Maupas and Seurat. The females can be distinguished from those of *N. dromedarii* by the position of the vulva, which is located in the posterior body-region in the former species, while in the latter it is situated one-third of the body-length from the anterior end.

(1d-54)

**Note on the Finding of Anchylostoma Duodenale in the Intestines of the Pig.**

*John Legg and J. A. Rheuben, M. J. Australia, 2:398, Sydney, Nov. 5, 1921.*

During July last a small number of pigs from Cromarty was killed, and in accordance with the usual practice the intestines were examined for parasites. In 3 of the animals nematodes closely resembling *Anchylostoma duodenale* (man) were found attached to the mucous membrane of the duodenum. The pigs in question were semi-domesticated. The discovery of *Anchylostoma duodenale* in pigs in North Queensland seems so important that experiments should be made to ascertain with what facility pigs can be infected from human sources.

(1d-54)

(1d—55)

**A Simple Levitation Method for the Detection of Hook-worm Ova.**

*H. Hastings Willis, M. J. Australia, 2:375, Sydney, Oct. 29, 1921.*

Hookworm ova will float in a salt solution of sufficient specific gravity, and will adhere to a glass surface with which they come in contact. A saturated solution of coarse sodium chlorid in tap water has a specific gravity of about 1.130 and is cheap, readily prepared and of sufficient density for the purpose. A saturated solution of magnesium sulphate is also easily obtainable and has a higher specific gravity, but is a little more expensive. The method presented is first to remove sufficient of the specimen, which has been collected in a small tin or an ordinary metal match-box, so that the container is not more than one-sixth full. The salt solution is added drop by drop and thoroughly mixed. Sufficient of the solution is added to fill the container to the brim. After waiting a few minutes to allow the ova to rise, a clean polished slide is placed on the container in contact with the surface of the fluid. After a few minutes, this is gently removed, inverted and examined under the microscope with a magnification of 100 diameters. If it is negative, a second slide is placed on the brim of the container and similarly examined. A distortion of the ova is liable to occur if they are left in the fluid over half an hour. As a rule, larvae will be found to float in the salt solution, which in a short time kills them.

(1d—56)

**Strongylid Parasites of Horses in the Punjab.**

*C. L. Boulenger, Parasitology, 13:315, London, Nov., 1921.*

A large number of parasitic worms of horses, both from Lahore and other districts of the Punjab, were examined, and referred to 21 species; while this is obviously not a complete list, it includes practically the majority of species of common occurrence in the Punjab. No new forms were obtained, but the report gives additional information on the structure and development of some of the less known species as well as remarks on their geographic distribution. Detailed descriptions of the various species are given.

(1d—57)

**On the Zoological Status of the Polymorphic Mammalian Trypanosomes of Africa and Their Relation to Man.**

*H. Lyndhurst Duke, Parasitology, 13:352, London, Nov., 1921.*

Reference is made to similar work carried out on the polymorphic trypanosomes of mammals. The species of trypanosome and the tendency to split the species into strains is considered at length. The glossinae play a most important rôle in transmission of trypanosomes. The direct and indirect method of transmission is discussed. The subject is discussed under 5 heads; Part 1 is concerned with the etiology of the Uganda Epidemic. It is not known whether the epidemic was started by the entry of *T. gambiense* from some neighboring endemic focus or was due to an already existent organism. An organism described as *T. gambiense* was present in the blood of an enormous number of human beings in the G. palpalis area of Uganda Lake. A relatively large percentage of the wild fly must have been cyclically infected with the human trypanosome. The experiments in part 2 on

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the infectivity of wild lakeshore flies, 1920-21, are given in detail, with a résumé of previous experiments on the lake-shore infectivity in Uganda. In part 3 the experiments involve the reaction of the monkey, sheep, dog, guinea-pig and rabbit to trypanosomes. The direct-transmission experiments of part 4 show that to the eleventh passage, there is no sign of any loss, on the part of the trypansome, of capability to undergo cyclic development in the fly. There is no evidence to prove that the virulence of a strain is enhanced by continued passage by direct transmission in the same animal. When trypanosomes are in the peripheral blood, direct transmission is likely to operate. In part 5 are described the experiments with laboratory-bred flies and the lake-shore and human flies, which were undertaken to ascertain the extent to which the 3 strains were transmissible by laboratory-bred *G. palpalis*; and further, to investigate the effect of different kinds of blood on these strains during their development in the fly.

In any strain of trypanosomes, the physiological characters (including ability to infect man) are largely determined by the environment. Further, all the polymorphic mammalian trypanosomes of Africa belong to a single species, and not to a multitude of species. This species is characterized by its polymorphism in its vertebrate hosts, and its anterior station in the salivary glands of its *Glossina* intermediary. Included in this species are many different varieties or strains, distinguishable from one another by characters of minor importance. These strains are not immutable, but variable, and are determined by the environment.

(1d-58)

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Lappeted Anoplocephala in Horses.

*Warrington Yorke and T. Southwell, Ann. Trop. Med. & Parasitol., 25:249, Liverpool, Sept. 30, 1921.*

The writers describe in detail the *Anoplocephala rhodesiensis*. They redescribe the *A. perfoliata* (Goeze, 1782, Blanchard, 1848), because the differences which were considered to be of specific value were of inconstant occurrence, and because this species exhibits considerable variation. In the specimens of *A. perfoliata* examined by the writers, the cirrus pouch extends over the longitudinal water vessel and nerve to the edge of the segment just as in the worm from the zebra. The relative position of the outer seminal vesicle and the cirrus pouch is inconstant, and finally the aporal wing of the ovary is about twice the size of the poral wing in both worms. The only constant points of difference between the lappeted *Anoplocephala* of the zebra and the horse, viz., *A. rhodesiensis* and *A. perfoliata*, are as follows: (1) *A. rhodesiensis* is much more massive than and has almost twice as many segments as *A. perfoliata*. (2) The posterior half of the former is entirely sterile, whereas in the latter the segments become increasingly ripe up to the posterior extremity of the worm.

(1d-59)

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Observations on the Ceratopogonine Midges of the Gold Coast with Descriptions of New Species.

*Henry F. Carter, A. Ingram and J. W. S. Macfie, Ann. Trop. Med & Parasitol., 25:177, Liverpool, Sept. 30, 1921.*

The writers describe at length the appearance, organs, eggs and  
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larvae of the genus *Dasyhelea* and the following species of that genus: *D. pallidihalter*, *D. fusciscutellata*, *similis*, *D. luteoscutellata*, *D. inconspicuosa*, *D. nigricans*, *D. flava*, *D. flaviformis*, *D. fusca*, *D. nigrofusca*, *D. fusciformis*. The pupal and larval stages are given much consideration. The habitat and the resemblances between the various species are noted.

(1d—60)

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**The Influence of the Hydrogen-Ion Concentration in the Development of Mosquito Larvae.**

*Malcolm E. MacGregor, Parasitology, 13:348, London, Nov., 1921.*

When mosquito larvae are brought to laboratories, they often fail to develop normally. After an exhaustive series of experiments varying the organic content of the water, in which the mosquito larvae were grown, tests were made of various waters, namely tap, local stream, pond and tree-hole waters, in terms of the hydrogen-ion concentration. The details of these experiments and of those on the changes in the pH affecting parasitic saprolegnia are described. The abnormal development of mosquito larvae in the laboratory may not be entirely due to changes in the hydrogen-ion concentration, but this nevertheless has a profound effect upon their metabolism, and on their resistance to diseases. Since their successful development is so adversely affected by changes in the reactions of the water in which they normally live, it may be possible by employing measures that will make the water of ponds acid, and the water of tree-holes alkaline, to find that this is another means of combating mosquito development.

(1d—61)

(1d—61)

**A New Philippine Mosquito (Diptera, Culicidae).**

*C. S. Ludlow, Mil. Surgeon, 49:690, Dec., 1921.*

Among the mosquitos sent to the Army Medical Museum during the summer of 1921, is an apparently new stegomyia, taken at Fort Wm. McKinley, which somewhat resembles the lately described *Stegomyia christiana* Dyar from China and the Philippines, but shows definite points of difference. The female head is very dark brown, practically black, covered with black and white flat scales, and a few black fork scales near the nape. The prothoracic lobes are widely separated, black, with a few white flat scales and dark bristles. The abdomen is partly denuded, brown, but paler than the mesothorax, covered with thin light brown, transparent scales, with a light border and lateral bristles. The coxae are dark, the trochanters light. All the femurs are dark-scaled with a marked sprinkling of white scales on the dorsal aspect and a small white apical spot. Ventrally they are light, rather a sordid white, nearly to the apex, with a brown portion just preceding the apical white spot. The wings are fuscous with brown scales, except at the base of the costa, where there is a small white spot. The length is about 5 mm. without proboscis, wing 4 mm. The white, flat scales on the mesonotum would place this species in Theobald's *kingia*, but in the classification at present recognized the species is thrown into *stegomyia*.

(1d—62)

**The Feeding Habits of Stegomyia Calopus.**

*R. Montgomery Gordon and C. J. Young, Ann. Trop. Med. & Parasitol., 25:265, Liverpool, Sept. 30, 1921.*

Brief reference is made to previous investigations on the time of feeding and the age at which Stegomyia calopus bites man. Experiments were made to investigate the feeding habits under as natural conditions as possible. Mosquitos were hatched in the laboratory at Manáos and kept in wire gauze cages, males always being present. The females were allowed to feed to repletion on the experimentors during the hours of daylight. They were marked, replaced in the cage, and kept for not less than fourteen days, sugar being available as food, during the last two or three days of this period they were again given the opportunity to feed during daylight from man. The first experiment showed that 31 of the marked female stegomyias were released at night not less than fourteen days after their first blood meal. During the succeeding four days, five marked and 3 unmarked fed during daylight. One was observed to feed at night. The second experiment showed that with the exception of 2 unmarked Stegomyia none were observed to feed. A third experiment demonstrated that 50 marked female Stegomyia were released during the daylight not less than fourteen days after their first blood feeding. During the succeeding four days, 10 marked and 10 unmarked fed during daylight, and 6 marked and 8 unmarked fed during the night. These experiments prove that Stegomyia calopus will bite either by day or by night, over fourteen days after their first blood meal, while under no artificial restraint and having opportunities of selecting day or night for feeding.

(1d—63)

**Microbicidal Action of Vapors of Certain Vegetable Essences.**

*A. Morel and A. Rochaix, Compt. rend. Soc. de biol., 85:861, Paris, Nov. 12, 1921.*

The "thread" method of Koch was used. Bacteria were exposed to the vapors of a number of essential oils, obtained by heating to a temperature of 37° C. The following bacteria were used: meningococcus (type B), Eberth's bacillus, Staphylococcus aureus, Bacillus diphtheriae, and anthrax spores. One cubic centimeter of each of the following essences was placed in the bottom of a test-tube—the thread, bearing the culture, being suspended so that its lower end was 3 cm. above the surface of the essence—lemon, thyme, orange, bergamot, juniper, clove, citron, lavender, gomenol, mint, rosemary, santal, eucalyptus an anise. *Conclusions:* (1) The effects varied; (2) the essences whose vapors were most active were lemon, thyme and orange; (3) sterilization was effected only by prolonged contact, even with sensitive bacteria. A considerable number of hours was necessary to kill the Bacillus diphtheriae, (seven hours with lemon and bergamot, twenty-four with thyme, orange and gomenol). The anthrax spores were not affected.

(1d—64)

**Bactericidal Action of Salts of Tellurium and Selenium.**

*Alfonso Cavazzuti, Ann. d'igiene, 31:551, Rome, Sept., 1921.*

Experiments were made to determine whether the salts of tellurium  
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and selenium have bactericidal action in vitro. A 0.25% solution of sodium tellurite was effective against all the bacteria tested except anthrax spores. It took effect on *Bacillus coli* in one hour and on *Pyogenes aureus* in ten hours. A 10% solution of sodium tellurite had a more powerful bactericidal action, killing staphylococci in one-half hour. Sodium selenite in 0.25% solution had only a slight, or absolutely negative, bactericidal action. *Cholera vibrios* were killed in 580 hours. A 10% solution, however, killed cholera vibrios in forty-three hours. A 10% solution of potassium selenite had an effect about like that of a 0.25% solution of sodium tellurite. It killed *pyocyanus* and *typhoid bacilli* in five and eight hours. When the salts were used in several successive experiments they gradually lost their bactericidal power. This accords with the findings of Gosio and Klett that bacteria have a reducing action on solutions of these salts, due to absorption of minute particles of the salts by the bacteria themselves. In this way the salts are necessarily reduced in concentration and their bactericidal power is decreased.

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## 1e. IMMUNOLOGY, SEROLOGY AND HEMATOLOGY

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### Old and New Knowledge of Immunity.

*Ludwig Hektoen, J.A.M.A., 77:1935, Dec. 17, 1921.*

The history of immunology may be divided into two periods: the premicrobic, from remote times to about 1880; and the microbial, or modern period, from 1880 to the present. The writer reviews the development of our knowledge of immunity from the time before the Christian era, through the early part of the 19th century, to the modern period in immunology.

The microbial period begins with the memorable demonstrations by Pasteur. We know now that there are two chief forms of immunity: (1) the antitoxic and (2) the antimicrobial. The establishment of microbial etiology settled for all time that there are specific diseases due to specific causes.

A lengthy discussion is given of streptococci, as these constitute the largest group of pathogenic bacteria. It is emphasized that by virtue of the specific relations between proteins and their antibodies, which are the essence of immunity, results of significant promise are being obtained in the field of streptococcus infection.

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### On the Essential Identity of the Antibodies.

*Hans Zinsser, J. Immunol., 6:289, Sept., 1921.*

Since Ehrlich's classical analysis of antibodies, it has been generally accepted in immunology that agglutinins, precipitins, sensitizers, bacteriolysins, hemolysins or so-called amoebocytes, opsonins and the anaphylactic antibodies are distinct substances formed in the animal body, often in response to treatment with a single antigen. Kraus has summarized this point of view clearly: "Just as the bacterial body contains a variety of different antigens, so we may assume that animal protein is made up of different antigenic elements. If the animal body is treated with such substances and finds corresponding receptors, there results the formation of a variety of qualitatively different antibodies."

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After an extensive review of the literature and a large amount of experimental work Zinsser concludes that while the "unitarian" view is not absolutely and rigidly proven further evidence should be awaited before denying the correctness of the view. Belief in the "unitarian" view has been maintained for a number of years, and teachers have considered it the most likely. While it cannot be proved, because of the difficult experimental problems involved, the theory has advanced far enough certainly to justify throwing the burden of proof upon those who still cling to the conception of separate structure for the various antibodies.

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**Antigenic Principle of the Erythrocyte.**

*F. Chodat, Compt. rend. Soc. de biol., 85:735, Paris, Oct. 22, 1921.*

Antigenic properties reside in substances of the erythrocyte which are insoluble in distilled water (stroma). Hemoglobin is not antigenic. Two questions are involved: 1. Is the substance in the erythrocyte which absorbs alexin in presence of the appropriate antibody exactly definable? 2. Is its action demonstrable after it has been extracted and isolated? The author has experimented with horse corpuscles washed at least four times, with physiologic salt solution, 7.5 to 1,000, and with the red cells of rabbits, goats and guinea-pigs. Laked erythrocytes are centrifuged, and the liberated stroma is agglutinated and precipitated by CO<sub>2</sub>. Theoretically, the stroma may carry down with it an undetermined, amorphous substance constituting the antigenic element of the red cell. Filtration of dissolved globulins removes the antigenic property. Experiments by Schmidt and Bennett have been carefully checked, using corpuscles of the goat instead of ox corpuscles. The precipitate owes its antigenic properties to the contained stroma, and not to globulins, which do not possess antigenic properties.

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**The Antigenic Properties of Organic Lipoids.**

*Paul Niederhoff, Deutsch. med. Wchnschr., 47:1204, Berlin, Oct. 27, 1921.*

The experiments of Forrsmann show that the heterogenetic organ-extracts from guinea-pigs and horses, and the red blood-corpuscles of sheep, produce the same antibodies. The Sachs-Guth flocculation reaction depends on the fact that the serum of a rabbit, which has had the intravenous injection of guinea-pig suspension, also produces antibodies against the sheeps' red blood-corpuscles, and is capable of dissolving them. The author has investigated the chemical properties of the flocules, which are found on the demonstration of heterogenetic antibodies by the Sachs-Guth reaction and also by the Sachs-Georgi and Meinicke syphilis reactions. The author injected the precipitate from an alcoholic extract of guinea-pigs' kidneys into the veins of a rabbit, in order to test whether the serum of the rabbit thereby assumes the property of precipitating the homologous extract lipoids used in previous treatment. The serum of rabbits, previously several times treated with pure lipoid, neither causes flocculation in the guinea-pig kidney extract nor lysis against the red blood-corpuscles of the sheep. Further rabbits injected with a mixture of lipoids and gelatin showed in their serum neither lipoid flocculation nor hemolytic properties. On the other

hand, the serums of rabbits treated with aqueous guinea-pig kidney extract, possess both flocculant and hemolytic properties. The name antigen for the pure alcohol-soluble portions is, therefore, incorrect. The aqueous extracts, however, contain bodies besides the lipoids, which bodies are extracted from the cells and retain their original form. These are the actual antigens. The experiments preclude the possibility of fatty antibodies being formed, but naturally others, such as fermentation bodies, may appear. It has not been proved, by careful study of the facts, that because heterogenetic immune serum (e. g. sheep-blood-dissolving rabbit serum) will flocculate added extract-lipoid (e. g. lipoid from guinea-pig extract) the active antibodies are thereby produced through pure lipoids. This is actually not the case, and even less probability supports the assumption that the anticomounds of the positive syphilitic serum, simply because they flocculate added lipoid extract, are of pure lipoid origin.

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**A Clinico-Philosophic Interpretation of Immuno-Therapy.**

*G. H. Sherman, New Orleans M. & S. J., 74:398, Dec., 1921.*

Immunity may be natural or acquired. Natural immunity may be explained on the theory that the non-specific protective ferments contained in the blood-serum of one species will digest and destroy organisms that may be able to live and cause disease in some other species. Acquired immunity may be obtained by the tissue cells becoming sensitized for the production of specific protective ferments as a result of an infection or inoculation. A passive immunity may be brought about by injecting immune serum obtained from some immunized animal. The severity of an infection depends upon the virulence of the infecting organism and the resistance of the host. The fundamental principle of immunity produced by inoculating attenuated organisms is employed in prophylactic inoculations against small-pox. Here a closely related non-virulent organism is inoculated, and the immunity thus established also protects against infections with small-pox. In applying bacterial vaccines, the principle of hastening immunization by injection of attenuated organisms is carried forward to the point of killing the organisms used. By this therapeutic measure, active immunization may be hastened during the course of an infection. Chronic infections are a condition in which the cells of the host develop a certain tolerance to the presence of microorganisms. This is due to a certain resistance offered by the invading organism to destruction by antibody formation, specific sensitization not being developed to a point of sufficient intensity to eradicate the infection. Here vaccine inoculations are clearly indicated.

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**Regarding the Equivalence of Vaccines.**

*J. Marais, Paris méd., 11:421, Nov. 26, 1921.*

The dogma of specific immunity has been somewhat shaken of late years by successful results obtained by "collateral" or non-specific immunization. This tendency, however, should not be exaggerated, as the following case tends to show: A patient with osteomyelitis and secondary arthritis of the knee which at first had been considered as a staphylococcus infection, was treated for several days with anti-staphylococcus stock vaccine with no result whatever. The patient was  
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then operated on. The local symptoms diminished, but the general condition remained bad. In the meantime it was discovered that the infection was really due to a streptococcus from which a vaccine was prepared. The administration of this was followed by rapid local and general improvement.

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**Effect of the Injection of Washed Platelets on the Elimination of Microörganisms Circulating in the Blood.**

*P. Govaerts, Compt. rend. Soc. de biol., 85:745, Paris, Oct. 22, 1921.*

It was conjectured that a diminished number of blood-platelets within the blood should produce less rapid elimination of microörganisms injected into the circulation. Antiplatelet serum was used as a probably satisfactory substance for experiment on guinea-pigs. The results were not as expected, typhus bacilli being eliminated somewhat more rapidly than in normal animals. To explain the unexpected results, washed platelets were injected intravenously into two guinea-pigs, after introducing typhus bacilli into the circulation of both animals. In the first animal, injection of the platelets was followed by injection of a suspension of erythrocytes; in the other animal, a primary injection of the erythrocyte suspension was made, the platelet injection following. Elimination of the bacilli was clearly and constantly more rapid after injection with the platelets. A new argument is thus adduced in favor of the antixenic function of the platelets.

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**Influence of Small Doses of Peptone on the Elimination of Microörganisms Injected into the Circulating Blood.**

*E. Delcourt-Bernard, Compt. rend. Soc. de biol., 85:738, Paris, Oct. 22, 1921.*

Non-virulent microörganisms, when injected into the circulating blood, are immediately eliminated by agglutination with platelet masses, transportation to the liver and subjection to phagocytosis. Abrupt introduction of peptone into the veins produces colloidoclastic shock, with almost complete disappearance of the platelets. Antecedent injection of peptone should therefore result in diminished or retarded elimination of the microörganisms. The study is rendered difficult by the induced arterial hypotension; moreover, rabbits resist peptone. In the experiments described, small quantities of peptone were gradually injected into guinea-pigs and rabbits. It was determined that small doses of peptone diminish mutual affinity of the platelets. Elimination by the platelets is independent of their mass volume. The two phenomena, formation of platelet masses and adhesion of the microörganisms to them, are not necessarily parallel. Even small doses of peptone promote phagocytosis of the staphylococcus in the blood of rabbits and guinea-pigs.

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**Antixenic Function of Plasma, Globulins and Platelets.**

*J. Roskam, Compt. rend. Soc. de biol., 85:733, Paris, Oct. 22, 1921.*

Protection against foreign bodies in the blood-stream is a physical (colloidal) process. The author has experimented with various brands (Sec. 1—Page 127)

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of Chinese ink. Globulins required repeated washing in order to obtain no agglutination. Agglutination by the globulins does not depend on the globulins themselves, but on a layer of plasma adhering to their surfaces. Antixenic function is a plasmatic function. Agglutination is only an evidence of changes in colloidal equilibrium of the plasma, determined by contact with the surface of a foreign particle. The phenomenon may serve as the basis of a test for thermolabile, physio-pathologic properties of washed globulins.

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**The Bacteriophagus; Its Unity; Its Lysin.**

*F. d'Herelle and G. Eliava, Compt. rend. Soc. de biol., 85:701, Paris, Oct. 22, 1921.*

Given the serum of a rabbit prepared by a series of injections with cultures of the antidyserenteric bacteriophagus, it is difficult to prove the presence of a sensitizer specific for the antidyserenteric bacteriophagus. A culture of the bacteriophagus can only be a suspension of ultramicro-organisms in a liquid containing the dissolved cell-substances of dysentery bacilli at whose expense the ultramicroörganisms have developed. Serum from the injected animal contains two sensitizers, one specific for the dysentery bacillus, the other for the ultramicroörganisms. The two are inseparable. Complement fixation will always occur and it will be impossible to know which of the two antigens is responsible. The problem must be solved otherwise. If the bacteriophagus is really monobacterial, the sensitizer in the antidyserenteric bacteriophagus serum should be fixed by all bacteriophagi. Proof of the presence of a sensitizer would then be possible, for in working with a culture of bacteriophagus other than the antidyserenteric variety the reaction would not be disturbed. A culture of antiplaque bacteriophagus is a suspension of ultramicroörganisms in a liquid containing the dissolved cell-substances of *Bacillus pestis*. The only element common to cultures of antidyserenteric and antiplaque bacteriophagi can be the bacteriophagi themselves. The element in antidyserenteric bacteriophagus serum capable of affecting a given culture can be only a sensitizer for the one element common to all cultures of the bacteriophagus, the bacteriophagi themselves. Facts support this hypothesis. Antidyserenteric bacteriophagus serum contains a sensitizer specific for the bacteriophagus, whatever the culture and bacterial species on which the bacteriophagus may have acted. The bacteriophagus is an entity, an autonomous living being. Its vital character is indicated by previous experiments in which lysins causing its effects were actually isolated. It is now proved that the bacteriophagus is an ultramicroörganism, a parasite of bacteria and capable of adaptation to the most varied bacterial species (parasitism). A work now in press will contain the complete protocols.

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**Bacteriophagus within the Organism.**

*R. Appelmans, Compt. rend. Soc. de biol., 85:722, Paris, Oct. 22, 1921.*

The fate of the bacteriophagus within the body has been studied in guinea-pigs and mice. The bacteriophagus is not a bacterial variation, but a distinct entity. It is not resorbed by the digestive tract. If injected, it rapidly reaches the blood and is eliminated in the urine and

stools. It usually persists in the spleen for about two weeks. The author believes it is destroyed by an antibacteriophageic agent developed within the organism.

(1e—12)

**Inhibitive Effect of the Bacteriophageic Principle on the Development of Susceptible Microorganisms.**

*J. De Necker, Compt. rend. Soc. de biol., 85:742, Paris, Oct. 22, 1921.*

If a few drops of bacteriophageic filtrate are added to a tube of bouillon and a bacterial culture be added, the susceptible microorganisms do not seem to develop, at least no clouding of the bouillon results. The bacteria are thus apparently inhibited in growth until they have acquired resistance to the bacteriophagus. To determine whether the bacteriophagus is really inhibitive or whether the bacteria merely die as they develop, two rabbits were injected, one with killed cultures of d'Herelle's bacillus, the other with an emulsion of Voldagsen's bacilli. It was concluded that the bacteriophagus really inhibits the growth of susceptible bacteria.

(1e—13)

**The Bacteriophageic Ultramicroorganism.**

*F. D'Herelle, Compt. rend. Soc. de biol., 85:767, Paris, Oct. 29, 1921.*

Recent theories are discussed in the light of the author's work. Three hypotheses have been suggested: (1) A substance, or "principle," destructive to invading bacteria, is elaborated by the host (Kabeshima). The continuous action observed disproves this theory, for the causative agent does not become exhausted. Bordet suggests that a substance is manufactured inducing a tendency to lysis in bacteria. However, the author has worked with 3 series of 4 guinea-pigs each, as suggested by Bordet, without finding an anticolon bacillus bacteriophage in the peritoneal exudate. Bordet's result was accidental; if a large quantity of an active culture of the bacteriophagus is fed to the animal coincidently with the last injection, the result is always positive, the bacteriophagus ingested (about 2 c.c. of the culture) being active against the injected bacteria. Bordet's theory is really related to the second hypothesis. (2) The origin of the bacteriophagus is bacteriolytic, and it is therefore specific. The author thinks Bail's experiments insufficient; the results obtained by the author conclusively show that the bacteriophagus is not specific. (3) The bacteriophagus is an autonomous organism, ultramicrobic, and a parasite of bacteria. It has been shown that it consists of masses which can be counted, and that certain antiseptics (glycerin, quinin), which have no effect on diastases and toxins, sterilize cultures of the bacteriophagus. Hypotheses other than the third must be excluded.

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**D'Herelle's Phenomenon and the Fixation Reaction.**

*E. Wollman and L. Goldenberg, Compt. rend. Soc. de biol., 85:772, Paris, Oct. 29, 1921.*

This study supports D'Herelle's explanation of the bacteriophagus, without actually proving its correctness. The fixation reaction was  
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employed in two rabbits. By hypothesis, the bacteriolysate should contain two antigens, namely, that of the bacterium subjected to lysis and that of the dissolved bacteriophagus. By saturating the sensitizer corresponding to the dissolved bacterium, that corresponding to the bacteriophagus should remain. The bacteriophagus is not proved to be an entity, but the antigenic value of bacteriolysates obtained by the methods of D'Herelle is clearly shown. Such bacteriolysates should be useful in the fixation reaction, especially with microorganisms not so readily autolyzable as Shiga's bacillus.

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**Identity of the Phenomena of Twort and D'Herelle.**

*A. Gratia and D. Jaumain, Compt. rend. Soc. de biol., 85:880, Paris, Nov. 12, 1921.*

The authors have confirmed results reported by Twort, which are identical with those described by d'Herelle. In the authors' experiment with transmissible lysis of streptococci it was necessary to overcome the resistance of staphylococci of various types and origin. The lytic principle obtained is not equally active in all types. A strain which is very sensitive and capable of dissolving in large quantities, in a given volume of bouillon, should apparently furnish an active filtrate; this is not the case. The filtrate from a solution containing 6 agar cultures in 100 c.c. of buillon was not especially active. Cultures of staphylococcus may sometimes be completely destroyed, but perfect sterility is not usual; an incompletely sterile culture reproduces vigorously. On recultivation, waves of growth and dissolution may be noted, equilibrium being finally reached. As with other species, a trace of lyticized culture produces irregular, vitreous lysogenic colonies on agar and also regular, opaque and non-lysogenic colonies. The appearance of the latter may be very variable. These phenomena are the same with *bacillus coli*. Non-lysogenic cultures tend to degenerate. Possibly the condition is one of larval lysis.

(1e—16)

**Studies on the Phenomenon of D'Herelle with *Bacillus Dysenteriae*.**

*Martha Wollstein, J. Exper. Med., 34:467, Nov., 1921.*

The phenomenon of d'Herelle is the expression of a lytic reaction occurring between a bacterium which is inducing an infection in an animal and a substance elaborated in that organism. Further, whenever an animal offers resistance to a pathogenic bacterium, a bacteriophage active for that bacterium can be isolated from the dejections of the animal. The author's experiments show that a lytic fluid for dysentery bacilli can be obtained from the peritoneum of the guinea-pig by intraperitoneal inoculation of live dysentery bacilli. A lytic fluid with similar effects was obtained from a child dying of dysentery and an anti-colon-bacillus lytic fluid from a child dying of colon bacillus peritonitis. The presence of these lytic substances results in the formation of resistant strains of bacilli, which may be the ones responsible for the untoward outcome of disease in human beings.

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(1e—17)

**Disinfection Experiments with Bacteriophages.**

*Tai Watanabe, Wien. klin. Wchnschr., 34:522, Oct. 27, 1921.*

The bacteriophages cultivated by Bail were used in the experiments against the Flexner and coli bacilli from the stools of cattle. Carbolic acid in varying concentrations was added to the bacteriophages; after the disinfectant had acted for from one-quarter to six-fourths hours, small amounts of the carbolic-bacteriophage mixture (0.1 c.c.) were transferred into bouillon, and this was then contaminated with the particular bacterium (Flexner or coli). In this way it was observed that only the addition of 5% carbolic acid killed the bacteriophages after one and one-half hours. The coli bacteriophage was more resistant; it was only inhibited by 5% carbolic acid in one and one-half hours, but was not killed. Other disinfectants (salicylic acid and lysol) also produce a comparatively slight immediate inhibition, but destruction with difficulty, showing again that the coli bacteriophage is much more resistant than the Flexner bacteriophage. Alcohol (96%) had like effect. Even 0.8 c.c. of the mixture barely destroyed the immediate effect after one hour. A 10% soda solution inhibits the Flexner bacteriophages, 20% kills them; but this is not so with the coli bacteriophages. The sensitivity to sublimate is greater, but the author cannot make definite statements.

The bacteriophages hitherto tested withstand heating to 58° and even to 65° C. for one-half hour; 75° C. have a lethal effect. On the other hand, the bacteriophages are very resistant to desiccation. The great dissimilarity of the strength of the various bacteriophages renders judgment difficult, as it is not yet clear whether it corresponds only to quantitative or also to qualitative differences.

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**Sensibility of Adrenalectomized Rats to Toxins.**

*J. T. Lewis, Rev. Asoc. médica argentina, 35:131, Buenos Aires, Aug. 1921.*

In a former work it was stated that the sensibility of animals to tetanic or diphtheritic toxin was not altered by the removal of one suprarenal capsule; that the removal of both capsules at one time was fatal; that the bilateral operation, in two stages, with an interval of eight days, did not do serious harm to the animal. From this it was concluded that bilateral extirpation of the suprarenal capsules increased sensibility to tetanic toxin by suppression of adrenalin secretion. It is believed that adrenalin neutralizes this toxin in vitro. As this insufficient number of experiments seemed inconclusive a further series of tests was carried out to verify the former conclusions. It was found that the sensibility to morphin of adrenalectomized rats disappeared or was attenuated after a certain time, but in an irregular manner.

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**Notes on the Production of Immunity to Diphtheria Toxin.**

*A. T. Glenny and H. J. Südmersen, J. Hyg., 20:176, London, Oct., 1921.*

The writers noticed a marked contrast between the immunity response to the primary stimulus and the response to the secondary stimulus. "Primary stimulus" is the term applied to the initial injection of (Sec. 1—Page 131)

an antigen into a non-immune animal; "secondary stimulus" is the term applied to the injection of toxin into an actively immunized animal, while "intermediate stimulus" is the term applied to the injection of toxin into an animal that is only partially immune. The 3 stimuli are elaborated on at great length and contrasted with each other. The method of procedure, technic and doses of toxins injected are given. A large number of tables and plots of curves clarify the text. The animals used were guinea-pigs, horses, rabbits, goats and sheep. The first series of experiments were those in which toxin was injected into animals with no normal antitoxin. In animals possessing no normal antitoxin, a single injection of toxin either "attenuated" or under cover of antitoxin, whether injected previously or at the same time, or present in the form of passive immunity maternally transmitted, is followed by a latent period of about three weeks, and the maximum immunity is reached in about eight weeks. This is illustrative of the primary stimulus.

In the next experiments, toxin was injected into actively immune animals. These experiments proved that in immune animals, whether naturally or artificially immunized, a single injection of toxin-antitoxin is followed by a latent period of about four days and the maximum immunity is reached in about ten days; the great and rapid immunity response to the secondary stimulus offers a striking contrast to the small and gradual response to the primary stimulus. The injection of toxin into a partially immune animal acts as an intermediate stimulus. In partially immune animals, the response to an injection of toxin is, in magnitude and rapidity, of a character intermediate between the responses following a primary and secondary stimulus.

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**The Toxigenic Features of Strains of the Diphtheria Bacillus Isolated from Horses and from a Mule.**

*G. F. Petrie, J. Hyg., 20:99, London, Oct., 1921.*

Reference is made to Minett's investigations in which, from purulent discharges from horses, he isolated a number of diphtheroid strains including the bacillus of Preiss-Nocard and 12 strains of the diphtheria bacillus. Petrie experimented with 6 of these original cultures. The results obtained on the first attempt at toxin production are briefly as follows: Each of the 6 strains yielded a filtrate of which 0.1 c.c. killed a "250 gm." guinea-pig within forty-eight hours when injected under the skin. Later tests show that the M. L. D. of the various filtrates approximated to 1/100 c.c. more or less, and that a mixture consisting of equal volumes of each gave an M. L. D. of 1/100 c.c. Two hundred M. L. D.'s of the pooled filtrates when mixed with 5 units of diphtheria antitoxin and injected subcutaneously produced neither local nor general symptoms in a guinea-pig; this result demonstrates complete neutralization of the toxin by diphtheria antitoxin. The L plus dose of the several toxins from the 6 strains varied from 0.5 c.c. to 1 c.c. Intracutaneous tests of the individual toxins gave skin reactions with amounts corresponding with the relation known to exist between the subcutaneous minimal lethal dose and the intracutaneous minimal reacting dose of diphtheria toxin (1=1/500). These results confirm those of Minett's conclusions that the cultures are veritable strains of the diphtheria bacillus. These findings strengthen the views that horse diphtheria is

of practical importance in relation to public health and that the occurrence of the disease in horses throws light on the comparative frequency of "normal" antitoxin in their blood.

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**The Possibility of Discovering Experimentally the Presence of Diphtheritic Toxin in the Serum of Patients.**

*Pietro Busacchi, Riv. di clin. pediat., 19:331, Florence, June, 1921.*

The author performed experiments to test the validity of Uffenheimer's claim that serum from a diphtheritic patient if injected subcutaneously in the abdomen of a guinea-pig, causes a characteristic hemorrhagic edema which is to be considered the expression of a mild diphtheria poisoning. He used a constant amount of serum, 0.3 c.c. in 0.7 c.c. of normal salt solution, thus giving a constant volume of 1 c.c. He made tests on serum drawn both before and after serum-therapy had been used. He also made Romer's test in order to compare results. Of 14 cases examined, 4 gave a negative result in the animal under both conditions. Yet in 3 of the 4, the condition of the patient was so grave that the presence of an intoxication could not be denied. In another group of 3 the reaction was weakly positive before serum-therapy, negative after it. But the conclusions that might be drawn from these patients find no support in a third group of 5, in which the results were positive both before and after antitoxin was administered. We cannot admit that the positiveness is due to toxin left free in the patient's serum, for clear and decisive results by Romer's method contradicted this. In 2 cases of very severe intoxication, there was no reaction before the serum was given, but a positive one occurred fifty to sixty hours after such treatment. This result was wholly unexpected, for it could not be maintained that the diphtheritic toxin in the blood becomes more active after the treatment. Finally, serum was used from 2 healthy children who had recovered from diphtheria some time previous, and in whom there was no trace of infection; a clearly positive reaction was obtained in the guinea-pig. The author found such a reaction would result even if a considerable quantity of specific newly-developed antibodies were contained in the serum. Using common anti-diphtheritic horse-serum, he got reactions variously positive and negative. It is logical to suppose that human serum may, by its biological relation to that of the guinea-pig, cause irritation and pseudo-inflammation in the latter by its heterogeneous content. At all events, the results of the experiments leave no room for belief in the validity of Uffenheimer's test as it failed to reveal the presence of diphtheritic toxin in the blood of the patients.

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**Experiments on the Influence of the Universal Light Bath on the Action of Diphtheria Toxin within the Organism.**

*C. Sonne, Compt. rend. Soc. de biol., 85:759, Paris, Oct. 22, 1921.*

The minimum lethal dose of diphtheria toxin was injected into 38 guinea-pigs. One-half of the number were exposed to the light bath for two hours, and one-half served as controls. The source of light was an arc lamp of 50 ampères and 70 volts, the radiations being filtered through a glass chamber containing a layer of water 6 cm. deep, for arrest of the most important ultraviolet and infra-red rays. Three

animals were severely affected by the heat and were not included; three others sustained violent coryza and were also excluded. In the 13 animals represented in the report, the effects of the light bath in diminishing the activity of the toxin are clearly evident. The author believes that the toxin is more or less destroyed by elevation of the blood temperature from exposure to the rays. The experiments are tabulated.

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**Effect of Manganese Chlorid and Other Metallic Salts on the Formation of Diphtheria Antitoxin and the Agglutinin of *Bacillus Coli*.**

*L. Walbum, Compt. rend. Soc. de biol., 85:761, Paris, Oct. 22, 1921.*

The author considers catalytic action of metallic salts as a cause of the formation of antitoxins within the animal organism. If the hypothesis is correct, introduction of the particular salts should result in augmenting the process. Experiments were made with goats immunized against *Bacillus coli* and horses immunized against *Bacillus diphtheriae*. The salts employed with goats were manganese chlorid, nickel chlorid, cobalt chlorid and zinc chlorid. Each dose injected was 25 c.c. of the centinormal solution. With horses, the only salt employed was manganese chlorid, the dosage being 10 c.c. of the seminormal solution. The injections produced considerable increase of antitoxin in the blood. In the horse, the concentration declined despite repeated injections; but daily injections for two or three weeks usually resulted in augmentation. In horses frequently immunized and showing a decline in antitoxin production for some months, the injections sometimes produced a concentration of antitoxin exceeding that obtained by the usual immunization. Graphs are included with the report.

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**Antianaphylactic Shock and Colloidoclasis.**

*Auguste Lumière, Presse méd., 29:960, Paris, Dec. 3, 1921.*

This article answers some objections to the author's theory of anaphylactic shock which were recently made by Widal. The chief one is that the flocculation of serum which is supposed by Lumière to be at the basis of anaphylactic shock has never been demonstrated. This is due to the fact that the flocculated granules possess about the same density and refractive power as the surrounding medium, so that their detection even with the ultramicroscope cannot be expected. Agglutination may, however, be revealed by the use of various apparatus (agglutinoscope, seroscope, tyndallimeter, nephelometer, dispersimeter) which are based on the observation of Tyndall's phenomenon, and experiments made by several authors have shown that whenever the shock-producing property is conferred on a serum by appropriate treatment the seroscopic examination revealed the formation of a flocculation. Symptoms of acute or attenuated shock are the same whatever be their mode of production or the substance used, so that the process which causes the crisis must be the same in all cases. This is confirmed by experiments of the author which enable him to conclude that it is possible to vaccinate successfully against all possible anaphylactic or anaphylactoid shocks with injections of small quantities of any of the shock-producing substances.

It is difficult to conceive how barium sulphate, which is insoluble and completely inactive chemically, could act through the cellular envelopes in such a way as to disturb the colloidal equilibrium of the protoplasm, according to Widal's theory. It is possible to produce suspensions of particles of barium sulphate which are either uniformly distributed or flocculated together but contain the same number of particles and are absolutely identical from a chemical point of view. The first produces no untoward effect when it is injected into the heart of a guinea-pig, while the second always kills the animal. The different effect produced must therefore be due to the differences in the physical state of the suspension. The widely different substances which produce shock are not in any way related chemically, but they have one common physical property, the flocculation state, to which the phenomena of shock must logically be attributed.

Lumière's theory explains the phenomena of shock by supposing that the flocculates irritate the endothelium of the cerebral capillaries, which dilate in order to allow them a free passage. This vasodilatation is transmitted by reflex action to the splanchnic capillaries and the increase in volume of the vessels is the cause of the enormous decrease in blood-pressure. If this theory is correct, one should be able to avoid shock by preventing the sudden action of the flocculates on the endothelium of the capillaries of the brain. This is precisely what is accomplished by blood letting, ligature of the carotid arteries, and the injection of small doses of the shock-producing substance. The same results should be and are obtained by diminishing vascular excitability (anesthetics), by counteracting vasodilatation (with vasoconstricting substances) and by reestablishing an equilibrium between the volume of the blood vessels and that of the blood (injection of a large quantity of liquid into the circulation).

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**New Researches on the Influence of Anaphylactic Shock in Experimental Infections.**

*Fernand Arloing, A. Dufourt and L. Langeron, Bull. Acad. de méd., 86:309, Paris, Nov. 29, 1921.*

The authors' previous experiments have shown that sero-anaphylactic shock may protect guinea-pigs against a fatal pyocyanic infection in 80 to 88% of cases. The results of further experiments on 200 guinea-pigs are as follows: (a) Serum shock six hours after infection. No results obtained against infections caused by *B. anthracis*, *Pneumococcus* or *B. tuberculosis*; 30% and 15% of cures respectively in infections produced by *B. coli* and *B. typhosus*. (b) Peptone shock. No results in *pneumococcus* septicemia.

An attempt was made to attenuate a given strain of pneumococcus by passing it through several guinea-pigs when the animals were in a state of shock. This gave contradictory results but the virulence of the pneumococcus did not seem to be much affected. The general lack of success in these experiments is attributed to the difficulty experienced in not infecting the animals hopelessly, in producing a sufficient, but not mortal, degree of shock at the proper time, and to the greater resistance of encapsulated or sporulated organisms.

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**The Prophylaxis and Treatment of Colloidal Shock.**

*Auguste Lumière, Paris méd., 11:445, Dec. 3, 1921.*

Colloidal shock is due to the sudden irruption of flocculates into the capillaries of the nervous centers. These flocculates irritate the endothelium and produce a vasodilatation and fall of blood-pressure. Treatment and prophylaxis of shock should therefore be based on the following principles: (a) Avoidance of the formation or sudden introduction into the blood of a flocculate. In the case of anaphylactic patients this is accomplished by Besredka's desensitizing method (previous injections of small doses of the anaphylactogenic substance). Alimentary anaphylaxis can also be treated by the ingestion of small doses of peptone one hour before meals. As regards anaphylaxis toward milk, it should be noted that it is caused by the split products of casein and of the other proteins of milk. These are the substances which should be used to produce desensitization. (b) Dissolving the flocculate in appropriate reagents. Sodium hyposulphite, carbonate, acetate, tauro-cholate, glycocholate and chlorid have been used for this purpose. (c) Prevention of the sudden action of the flocculates on the cerebral vessels. This is realized by preventive vaccination with small doses, which renders the endothelium of the capillaries less sensitive to the mechanical action of flocculates. The same effect may be obtained by the injection of small quantities of a non-specific inert substance, such as barium sulphate.

(d) Diminishing vascular excitability. Although this does not appear to be a practical method, it has been found that doses of anesthetics which are too small to produce anesthesia can prevent shock. (e) Paralyzing reflex vasodilatation, e. g., with adrenalin. (f) Reestablishing the equilibrium between the volume of the dilated blood vessels and that of the blood. The injection of massive quantities of liquids appears to give the best results in acute shock.

Certain products which, like arsenobenzol, produce phenomena similar to shock do not seem to act by precipitating colloidal elements of the serum but through an elective action on the cells. When this action has taken place it cannot be made to disappear at once and these methods do not apply entirely. Their use must be limited for the present to true anaphylactic shock and to shock produced by flocculates.

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**Experimental Hemoclastic Shock and Edema.**

*J. Le Calvé, Bull. Acad. de méd., 86:226, Paris, Nov. 1, 1921.*

One centigram of indol and skatol was used to produce hemoclastic shock. Following the injection, leukopenia, vagotonic action, fall of blood-pressure, and a depressing effect on the sympathetic nerve were observed. Pathologic examination at various intervals showed hyperemia of the viscera and especially of the nervous centers and also edema in the latter. When, however, a peripheral stimulation was made elsewhere, for instance, by resection of a nerve or ligation of a vein, the edema appeared in that region, the theory being that it is localized in the territory where the vasomotor disturbance is greatest.

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**An Inquiry into the Nature of the Serological Difference Exhibited by Different Cultures of a Bacterial Species (Bacillus Typhosus).**

*A. Duncan Gardner and E. W. Ainley Walker, J. Hyg., 20:110, London, Oct., 1921.*

Previous experiments concerning the marked serologic differences among certain strains of *B. typhosus* are mentioned. The technic, methods of procedure and charts showing the results of the present experiments are detailed. The motile (T. M. and T. E.) and non-motile (T. Non. and T. O.) types of *B. typhosus* gave rise on inoculation, in all the animals used, to the production of serums which agglutinate to a greater or lesser degree both types of bacillus. T. M. and T. Non. present a marked "serological difference." In each of the 4 rabbits used, the serum obtained after a single inoculation, or after 2 inoculations of the same antigen, acted much more strongly on the homologous bacillus than on the heterologous type. The difference ranged from double to as much as twenty-fold. T. E. and T. O. showed a similar serologic difference, the range in this case ran to fifty-fold. T. M. and T. E. exhibited a completely homologous serologic character, and the same was true of T. Non. and T. O. For wherever T. M. is the more highly agglutinated of its pair, T. E. presents a similar relation to T. O., and the converse holds equally good. But T. M. and T. E. and T. Non and T. O. run together. In every case where a non-motile type of bacillus was used and antigen in the production of a serum, the serologic difference between the types was distinctly greater than where a motile antigen was employed. When, after 1 or 2 inoculations with one type of bacillus (motile or non-motile), a rabbit was inoculated with the other type of bacillus, its serum exhibited striking changes in relative agglutinating power. The titer always showed a notable increase for the antigen last injected. For the other antigen the naturally occurring fall frequently continued, though it may be arrested or even slightly reversed. In any case the ratios of the titers were always completely changed, this reversal or "cross over" is the most striking feature seen in the charts.

Experiments were carried out to test the agglutinative characteristics of the 2 types. In both rabbits treated with the non-motile form the serum produced had so extremely feeble an action on the motile forms that the readings could possibly be considered within the range of possible "normal" agglutination. This difference might be due to the idiosyncrasies of individual rabbits and not to the antigens used. In 1 of the 2 rabbits injected with a suspension of the washed motile form, the serum showed relatively high agglutination of the corresponding non-motile suspension (T. Non.), and actually agglutinated the other non-motile suspension (T. O.) in a much higher dilution than either of the motile suspensions (T. M. and T. E.). But a second rabbit, injected with the same suspension, gave a serum whose action was precisely similar to that of the serums produced by the injections of suspensions of unwashed motile forms in the first series of experiments.

(1e-29)

**Analysis of Agglutination in Typhoid Patients.**

*H. Rotky, Cntrlbl. f. Bakteriol., 87:16, Jena, Sept. 1, 1921.*

In research work on bacteria of the typhoid and paratyphoid  
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groups, Weil and Felix have demonstrated two different agglutinogens, as in earlier research they discovered two X strains. One of these agglutinogens is destroyed by heating to 100° C. The agglutinins corresponding to thermostable receptors produce fine flocculation of the homologous bacteria, the thermolabile ones coarse flocculation.

Experiments were then carried out to determine whether or not both these agglutinins were found in the sera of typhoid and paratyphoid patients, and if so, in what proportions. For this purpose a diagnostic serum for typhoid was prepared, which contained only agglutinogens producing fine flocculation. This was prepared by the method used by Bien and Sonntag in their experiments on X strains. A freshly prepared culture of typhoid bacilli was placed in 1.5 c.c. normal saline solution. To test the finely flocculating agglutinins of typhoid sera, one strain of fowl typhoid and one of Gärtners bacillus was used, as Weil and Felix and also Gruschka have found that the stable receptors of these three species are identical, and that serologically they are distinguished only by their labile receptors.

The results of the experiments which were carried out only with normal and typhoid sera showed that the normal agglutinins of human serum belong chiefly to the finely flocculating type. Of the patients' sera one group showed a low agglutination value or none at all, with alcohol typhoid bacteria, while unchanged typhoid bacilli were flocculated by relatively high dilutions. Fowl typhoid and Gärtners bacilli reacted only slightly.

The second group included cases at a later stage of the disease. These sera are much richer in finely flocculating agglutinins than those previously mentioned. Another group was made up of sera of patients who had been examined several times during their sickness and convalescence. In the latter there was a certain parallelism between the increase of finely flocculating and of coarsely flocculating agglutinins.

(1e—30)

**Relations of the Agglutinin Content of Maternal Milk to the Serum of Mother and Child in Typhoid Fever.**

*Hanns Löhr, Ztschr. f. d. ges. exper. Med., 24:371, Berlin, Sept. 22, 1921.*

The author has recently reported on a puerperal woman affected with paratyphoid fever. Immediately after delivery the agglutinin content of the milk was greater than that of the blood. Bacilli could be cultivated from the milk for a longer time than from the blood. Löhr observed a second patient with paratyphoid fever during the puerperium, where the milk had dried up. After six weeks, by means of an intramuscular injection of 5 c.c. of milk, lacteal secretion was started again for two days. This milk had an agglutination titer of 1 to 300, the serum 1 to 200; paratyphoid bacilli could be cultivated from the milk. Since the patient's blood, stools and urine had been free from bacilli for three weeks, the bacilli must have remained in the breast after the drying-up of the milk, being liberated by the renewed secretion. In illness occurring in the same house with this patient, the author observed 3 other paratyphoid-B carriers, whose milk and blood agglutinations were systematically tested for two months after confinement, and also the blood of the infants. Ehrlich has demonstrated a transference of antibodies from the milk to the child. He exchanged the young of actively

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immunized and non-immunized mice. The longer the immune mother nursed the young of the non-immunized mother the greater the immunity of the latter became. The author has made the corresponding test for human infants. All 3 had been persistent carriers, but 1 only had had fever. In all 3 cases the agglutination titer of the blood was determined before confinement. The confinement raised the titer (twice from 1:200 to 1:300; once from 1:100 to 1:200). In all 3 cases, the milk titer was higher (1:700; 1:3,000, 1:5,000), varying according to the varying concentration of the milk. Non-specific stimulating substances, given parenterally (caseosan and milk injections) invariably raised the agglutination power of the milk. There was no relation between the titers of serum and of milk. Apparently the mammary cells shared in forming the agglutinins, which is in accordance with the fact that the latter is a function of all cells. In all cases bacilli could be cultivated from the milk for a longer time than from the blood. A milk flow brought about by stimulation, after having stopped for some weeks, again contained bacilli, proving that the latter had remained latent in the gland tissue. The author gave new-born infants to be nursed by one of the bacillus carriers, the infants' mothers never having had typhoid fever. The agglutination titer of the umbilical blood, to paratyphoid B, was determined twelve hours postpartum. By non-specific stimulation, the agglutination titer of the nurse's milk was first raised as high as possible. Two of the 3 infants nursed 5 times in twenty-four hours, one 10 times in forty-eight hours. Transfer of agglutinins through the milk to nurslings is proven beyond doubt. In the first case, that of an infectious carrier who was not ill, the second stool of meconium of the infant contained numerous paratyphoid B. bacilli; its umbilical blood agglutination was 1:200. The child did not become ill, but excreted bacilli during the entire observation period of two months. Infection occurred from the vulva during labor (by way of the urine), but placental immunity prevented illness.

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**Agglutination Titer Following Repeated Intravenous Injections of TAB Vaccine.**

*C. H. Han and C. W. Young, China M. J., 35:400, Shanghai, Sept., 1921.*

Recognizing the fallacy of generalizations from one case studied, the writer summarizes this investigation as follows: (1) In the case of one patient inoculated with the repeated small doses of a vaccine composed of *Bacillus typhosus*, *B. Paratyphosus A*, and *B. paratyphosus B*, there was a response in the form of the formation of agglutinins. Agglutinins appeared first after eight days in the cases of *paratyphosus B*, after eleven days for *typhosus*, and after twenty days for *paratyphosus A*. (2) The agglutinin response to the *B. paratyphosus A* strain employed was weak throughout. The response to *B. typhosus* and *B. paratyphosus B* was stronger but varied both absolutely and relatively, although the dosage of *typhosus* was twice that of *paratyphosus B* throughout. (3) There appeared to be an increase in the titer for about sixteen days following an injection, followed by a decline. This was repeated 3 times during the course of these experiments, and was evident each time the intervals between the injections were sufficiently long.

(4) There seemed to be a difference in the response to two different lots of vaccine, especially as regards *B. typhosus*, but several factors were involved which were not controlled in this experiment.

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**Friedberger's Reaction in Typhus, Typhoid and Recurrent Fever.**

*Gabriel Delamare, Bull. Acad. de méd., 86:305, Paris, Nov. 29, 1921.*

Friedberger's reaction (injection of heated *B. proteus X 19*) was tried by Delamare in 5 cases of typhus, 14 of typhoid and 2 of recurrent fever. Although according to Friedberger it should be negative in typhus, 4 positive results were obtained locally in the 5 cases. One local reaction was also accompanied by a general reaction, although it was less intense than in typhoid. In this disease positive results were always observed. The general reaction was sometimes so severe that the test cannot be recommended as a routine measure. The 2 cases of recurrent fever gave also positive tests. It is noted that certain symptoms frequently seen in typhus, such as cyanosis, herpes and desquamation, were also observed in patients tested with *Proteus X 19*, so that it is possible that the symptoms are due to a secondary infection caused by this organism.

The *proteus* reaction of Friedberger appears to be far from strictly specific and cannot be relied on to make a diagnosis of typhus in a difficult case.

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**Agglutination in *Bacillus Coli* Modified by Phenol.**

*P. Fabry, Compt. rend. Soc. de biol., 85:886, Paris, Nov. 12, 1921.*

*Bacillus coli*, grown in media containing phenol, acquires the property of growing without producing indol. The agglutination characteristics of such "modified" bacilli were tested in comparison with those of the "unmodified" bacilli. Injections of "modified" and normal bacilli were made into guinea-pigs and rabbits. The agglutinins so formed were found to be specific, i. e., those produced by "modified" bacilli did not agglutinate normal bacilli and vice versa. The tests furnish new evidence of the highly specific properties acquired by certain bacteria in the course of immunization.

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**Agglutination Reaction with Antiplague Serum.**

*Sixten Hesser and Carl Kling, Upsala Läkaref. Förh., 36: No. 37, Stockholm, Sept. 1, 1921.*

As several cases of plague have been reported not only in Asia Minor, but also in several European countries and as a rat-plague has been observed in South America, a special section has been founded in the State Bacteriologic Laboratory of Stockholm for the study of plague and the preparation of antiplague vaccine. The authors have conducted the examinations. They obtained plague serum from the Serum Institute of Bern and had previously obtained 3 pest culture strains from Berlin. Before the agglutination reaction was tested the strains were examined as to their morphology, cultural and biochemical condition and also as to their virulence. It was found that the cultures

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had lost their virulence, although they were typical in other respects. It was also observed that none of these 3 cultures agglutinated with the serum obtained from Bern. The authors obtained new cultures from the Pasteur Institute in Paris, and also new plague serum from the same institute. They tested the Pasteur cultures and observed that they were both typical and virulent. The agglutination reaction of this Pasteur serum, however, was negative. The serum was tested with the 3 other plague cultures, but gave similar negative results.

The authors then immunized a rabbit with heat-killed plague bacilli and obtained a strongly agglutinating serum. Other experiments proved that a typically virulent plague culture may be deprived of its agglutinability by animal passage, but that it is possible to restore this ability by means of prolonged culturing. It was also observed that agglutinable strains may appear in a natural pest infection. The authors obtained plague cultures from 2 rats with the plague and observed that one of the cultures agglutinated only slightly with the serum, and that the other culture was totally inagglutinable.

On the basis of their experiments the authors believe that a negative agglutination reaction is not always an important factor in the diagnosis of plague.

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**Vaccination against Cattle Plague.**

*R. Van Saceghem, Compt. rend. Soc. de biol., 85:878, Paris, Nov. 12, 1921.*

The method in most common use, called simultaneous vaccination, consists in simultaneously inoculating the virus and injecting serum. If too much virus is given the serum may not attenuate the disease and the animal may die of the plague. If too little virus is given in proportion to the serum, the serum will neutralize the virus and immunity will not be established. The author prefers what he calls the differential method. The animal is inoculated with 0.1 c.c. of virus and the disease develops naturally. On the second day of the fever 50 c.c. of serum is injected into the jugular vein. There is no danger of neutralizing the virus as the serum is injected after the animal has begun to react to the virus and so its defensive forces are assisted rather than paralyzed.

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**On Prophylactic Inoculation against Measles.**

*S. Hiraishi and K. Okamoto, Japan Med. World, 1:10, Tokio, Oct. 15, 1921.*

As the causative agent in measles is still unknown, its prophylaxis is by no means certain. In the experiments here reported blood for inoculation was obtained from the median vein of a patient having a good constitution, free from syphilis and tuberculosis, and was taken between the period of first appearance of Koplick's spots and the height of the eruption. Under sterile conditions the blood was withdrawn into a syringe which contained a definite quantity of 2% citrated physiologic saline; it was then diluted to 100, 1,000 and 10,000 times with 1% citrated saline. The diluted blood was inoculated at the intrascapular region. Blood was used as fresh as possible, but sometimes it had been kept for forty-seven hours in a cool, dark place. About three weeks

was usually allowed before second inoculation. The minimum morbid dose was between 0.001 and 0.002 c.c. A prophylactic inoculation of 0.0001 c.c. of the infected blood proved harmless and gave degree of immunity. Immunized children both over and under 5 years of age had protective power against an injection of at least the minimum morbid dose, but not immunity against the natural infection. Those who had onset of symptoms four weeks after prophylactic inoculation had a milder course than those without inoculation. Further experiments are being made as to repetition of inoculation and increase of dose.

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Serum against Chancroid, Especially Chancroidal Bubo.

*J. Reenstierna, Compt. rend. Soc. de biol., 85:830, Paris, Nov. 5, 1921.*

Since the end of 1918, the author has been occupied with the preparation of a serum against *Streptobacillus Ducrey*, the bacillus of simple chancre. Ascending doses of killed and living streptobacilli were inoculated into the veins of rams, over a prolonged period. Serum so obtained fixes alexin (complete deviation), at least up to a quantity of 0.025 c.c. plus 0.25 c.c. of an emulsion of Ducrey's bacillus and a normal dose of alexin. The agglutinating value has not been exactly determined. The serum has been employed in about 100 cases of chancroidal bubo, of which most were ulcerated. Intragluteal injections of 10 c.c. resulted in improvement by the next day. In cases of gonorrhea treated with the author's antigenococcic serum, the gonococci, which are sensitive to heat, are more easily destroyed (in arthritis, for example) if the antibodies in the serum act when the patient's temperature is rising. This fact has been applied to treatment with antistreptobacillus serum. The author has used a preparation composed of serum plus dead bacilli, such as typhoid, which causes a rise in temperature.

*Results:* All buboes not previously incised, except 7, were cured in from five to ten days, the average time being a little more than a week. The effect is usually striking by the next day. As a rule, 2 injections were made, with an interval of four or five days. In a few cases 1 injection, in a few others, 3, were given. In no case has there been a relapse. The diagnosis of chancroid was erroneous in the 7 uncured cases. In ulcer, the usual treatment should be combined with the use of the serum. In incised bubo, accompanied by profuse suppuration and great loss of skin, the serum acts rapidly on the infiltration. The symptoms are: Chills, fever after the injection, great sensitiveness at the site of injection for several days, and sensitiveness in neighboring glands. The average duration of ordinary treatment is a month or more; the author's method reduces the duration to one week.

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Studies on Acute Respiratory Infections. X. The Nature and Value of a So-Called Precipitin Reaction as Applied to the Serologic Grouping of Streptococci.

*Charles Krumwiede and Eugenia Valentine, J. Immunol., 6:343, Sept., 1921.*

Barnes in a recent study on the cultural and serologic relationship of hemolytic streptococci reported that the serums of rabbits intensively immunized against the streptococcus give precipitin reactions with

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streptococcus antigens even in a serum dilution of 1:3200. The streptococci were grown in broth for forty-eight hours at 37° C. The cultures were centrifuged at high speed to sediment the cocci. In each test a constant amount (1 c.c.) of clear, undiluted supernatant broth antigen was added to an equal amount of the diluted antistreptococcus serum. These mixtures, as well as controls with normal rabbit serum and with uninoculated broth, were incubated at 37° C. for eight or ten hours, placed in the ice-box for two hours and then read. Sterility tests were made to eliminate the possibility of the precipitate being bacterial growth. Barnes's results seemed extraordinary to the authors, as in their experience the most potent serums, when added to concentrated antigens, give precipitin reactions only in dilutions of 1:100 or at most, of 1:200. After paralleling Barnes's work and checking it by the regular agglutination test it was concluded that the method is not a precipitin reaction, but that the reaction is due to the growth and agglutination of the cocci in the mixtures of broth and diluted serum. The results are essentially the same as those obtained by the ordinary agglutination method. The method is of no special value in the elimination of the factor of spontaneous agglutination which renders the serologic investigation of streptococci so difficult.

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#### Diagnostic Importance and Specificity of Cutaneous Inoculation with Trichophytin.

*H. Markert, Münch. med. Wchnschr., 68:1288, Oct. 7, 1921.*

Scholtz has commented on the fact that intradermal injection of an extract of trichophytin cultures causes marked reaction at the inoculation site in patients affected with deep trichophytosis. He states that similar reactions may be obtained in superficial trichophytosis which is markedly inflamed, but only if the solution injected is 10 times as strong (1 to 50). He has found that patients affected with lupus vulgaris react strongly and almost without exception to intradermal inoculation with trichophytin, but that this non-specific reaction seems to fail in late syphilis. The reaction to extracts of trichophytin cultures in various fungous diseases has been recognized, but it was not known that skin tuberculosis could produce it. This fact may depend on the non-specificity of the trichophytin reaction. The author undertook extensive study for the determination of 2 questions: (1) Does positive reaction to intradermal trichophytin inoculation occur in skin tuberculosis and other diseases in subjects without past or present trichophytosis? (2) Are positive cutaneous inoculations with trichophytin specific, i. e., what are the reactions of the subcutaneous test with tuberculin and trichophytin? Reactions occur in subjects with past or present trichophytosis, whether deep or superficial. Patients with cutaneous tuberculosis, especially lupus and other skin diseases, behave differently. In some cases of lupus there was a transitory reaction to trichophytin inoculation, disappearing in twenty-four to forty-eight hours. These "pseudo-reactions" were partially due to carbolic acid used in the dilutions. They did not light up after subcutaneous test with trichophytin or trichosykon, nor with old tuberculin. They are not specific and stand in no constant relation to tuberculosis. Intradermal inoculation with trichosykon produced no reaction, even transitory; trichophytin caused a reaction in other conditions as well as in skin tuberculosis. Tricho-

phytin-Höchst doubtless contains substances irritating to the skin, trichosykon-Kalle apparently does not. The latter is therefore preferable for diagnostic tests, since it seems to provoke no non-specific reaction. Certain cases of skin tuberculosis show reaction persisting for a longer time after intradermal trichophytin inoculation, but only after using a syringe which had been used for injecting old tuberculin. They are therefore due to old tuberculin remaining in the syringe. This fact may be positively demonstrated by subcutaneous test with old tuberculin and trichophytin, since focal reactions at the inoculation site are noted only after use of old tuberculin.

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**Tuberculous Antibodies. Results Furnished by Their Detection in the Serum of Patients and Their Significance.**

*P. F. Armand-Delille, Bull. méd., 35:866, Paris, Oct. 29, 1921.*

Among the newer antigens which have been recommended, the methylic antigen of Bocquet and Negre is to be preferred, according to the author. Calmette and Massol's method, using increasing doses of complement and permitting titration of the antibodies in the serum, is recommended and employed.

The serum of a certain number of patients was studied with Besredka's and the methylic antigen, which were about equally sensitive. On the whole the complement fixation reaction is strongly positive in a large proportion of advanced cases of tuberculosis; this percentage decreases with the severity of the disease, and in clinically healthy persons only weak or negative reactions are found. The reaction is therefore specific and in the majority of cases apparently proportional to the intensity of the tuberculous infection. The fixation reaction is not parallel to the skin-test and has not the same significance. The complement fixation reaction is probably positive only in fairly advanced caseous lesions, so that while it may be of help it cannot be relied on exclusively to make a diagnosis.

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**Decrease of Antibodies in the Serum of Tuberculous Patients after Artificial Pneumothorax.**

*P. Armand-Delille, Hillemand and Lestocquoy, Bull. Acad. de méd., 86:264, Paris, Nov. 15, 1921.*

The significance of the tuberculous antibodies which can be detected in the serum of patients by complement-deviation tests is not fully elucidated. It seems, however, that they do not represent an immunity reaction but are rather an indication of an active tuberculous process.

In the case of 5 patients who had relatively large quantities of antibodies before pneumothorax, a very definite, or even a considerable diminution, of these was noted after the operation, the proportions ranging between 5:3 and 8:1. This diminution was still observed in succeeding months and corresponded to the disappearance of fever and of general symptoms pointing to an active process. On the other hand, a patient who developed tuberculosis in the other lung after a pneumothorax showed a considerable increase of antibodies.

These facts are interesting inasmuch as they tend to confirm the  
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above-mentioned conception of the significance of tuberculous antibodies, and because they furnish another proof of the value of pneumothorax therapy.

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**Tuberculin.**

*C. Hartwell Cocke, Southern M. J., 14:965, Dec., 1921.*

Injecting tuberculin into a healthy animal gives a series of phenomena totally different from those resulting from injection into a tuberculous animal. Koch's accurate description of these is given. He observed that the tuberculin reaction is constitutional or general, focal, and local (at the site of injection). Since his pioneer work, it has become established that the reaction is specific, but specific only in that it indicates tuberculous infection, and not disease in the clinical sense, and hence is no criterion of activity. Though there are numerous tuberculins, similar in reaction, but varying in degree, the present discussion deals with Koch's original tuberculin, commonly known as O. T. Conclusions are: the reaction is an expression of hypersensitivity; tuberculosis does confer a genuine immunity, but it is only relative and for all practical purposes can never be considered absolute. The subcutaneous, cutaneous, and subconjunctival tests are described; reactions vary in each, and from all 3 tests it is apparent that failure to react is of vastly more importance, for upon this can be predicated the absence of an active tuberculous lesion—thus the test has more value in excluding tuberculous disease than in affirming its presence. Tuberculin is not as valuable in diagnosis as careful clinical and physical examination, as it indicates tuberculous infection and not disease. Though not a cure, it has a distinct beneficial effect upon certain cases.

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**Fixation Reaction and Tuberculosis.**

*J. Rieux and Ch. Zoeller, Presse méd., 29:881, Paris, Nov. 5, 1921.*

Three antigens are mentioned by the authors, which give about the same results, viz., Calmette's antigen, obtained by the maceration of tubercle bacilli in a peptone solution; Besredka's, which is prepared with a culture made on Besredka's egg medium, and finally the methylic antigen of Negre and Boquet, obtained by the action of acetone and methylic alcohol on tubercle bacilli.

The complement must be titrated. Most experimenters use heated serum, and place increasing doses of complement in contact with the same quantities of antigen and serum. It is universally agreed that this reaction, when it is properly performed, is specific. It is noted, however, that in syphilis and malaria positive results sometimes are obtained with tuberculous antigens. On the other hand acute diseases do not seem to modify the fixation test. Rieux and Zoeller also investigated 200 non-tuberculous patients, all except 19 of whom gave a negative reaction. Various percentages of positive results have been found in cases of clinical tuberculosis. The authors quote the results of several investigators and report 90 cases of their own, in which tubercle bacilli were present in the sputum, of which the fixation reaction was negative in only 3. In 27 cases of tuberculous pleurisy positive results were obtained 15 times. Six other patients with negative

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personal history and negative sputum were examined several times, and the test, which had been negative at first, became positive about two months after the beginning of the pleurisy. Six cases of tuberculosis of the peritoneum gave 4 positive reactions, and 49 of tracheo-bronchial adenitis gave 20 positive reactions. In tuberculosis of external glands and of the bones, between 17 and 70% positive results were found by other experimenters.

There is a category of cases in which tuberculosis may be suspected but not proved. The authors have collected 100 of these, in which the suspicion was founded upon a past hemoptysis, pleurisy, a pulmonary, osseous or glandular affection, or upon such symptoms as emaciation, slight fever and pulmonary signs. Fifty-two gave a positive test, and the greater the presumption of tuberculosis in each group, the higher was the percentage of positive results.

Generally speaking, a positive fixation test implies the presence of a tuberculous lesion having a certain degree of activity. In suspected cases it adds greatly to the probability of tuberculosis. In the case of a patient whose sputum becomes and remains free from tubercle bacilli, the test offers a warning that the cure is not complete and that further care is needed. Finally, it may reveal the tuberculous nature of certain affections of doubtful origin, such as polymorphous erythema nodosum. On the other hand, when the suspicion of tuberculosis does not rest upon anything very definite, a negative reaction justifies the exclusion of this diagnosis. When there have been recent presumptive signs (hemoptysis, pleurisy), it should be repeated, as it may become positive later.

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**Studies on the Tuberculin Reaction and on Specific Hypersensitivity in Bacterial Infection.**

*Hans Zinsser, J. Exper. Med., 34:495, Nov., 1921.*

A very full study of the rôle which anaphylactic sensitization to bacterial cell constituents might play in the symptomatology and pathology of infectious diseases, especially in their relation to the skin reactions with tuberculin, typhoidin, mallein, etc. There are 2 types of skin reaction, the immediate local response to intradermal injection and the late inflammatory reaction. The first type may be regarded as a manifestation of general hypersensitivity. From experiments with the injection of tubercle bacilli into guinea-pigs, he concludes that skin reactions and anaphylaxis do not necessarily coincide; that tuberculin hypersensitivity may develop independently of general tuberculin protein anaphylaxis. Further, there seem to develop 2 different forms of hypersensitivity in guinea-pigs infected with bacteria, typical anaphylaxis in which the protein material of the bacterial cells is concerned and a hypersensitivity to non-protein constituents. The attention of bacteriologists should be given to the non-protein constituents of the bacterial cell and they should produce the non-coagulable material from bacterial extracts to study the antibody-forming properties.

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**Researches on Regional Cutaneous Reaction.**

*Emanuele Mondolfo and Aldo Coscera, Policlinico (Pract. Sect.), 28:1571, Rome, Nov. 21, 1921.*

Experiments were made on 82 patients to confirm Pisani's results in comparing cutaneous reactions in the region of the tuberculous focus with those made in the arm. From the author's tabulated results it is concluded that the regional test is of great clinical value in suspected cases. The regional test can reveal a focus earlier and with greater intensity than the forearm reaction. Thus it may make it possible to prevent a new infection from progressing further. The regional reaction comes more quickly than that of the forearm; to compare their intensity, it is necessary to wait somewhat for the latter to manifest itself. In certain cases the arm showed an altogether negative result, when the regional test was positive. Oftener both reactions occurred, but the regional was much more marked both in the papule and the induration; in several cases it produced a peripheral ring that was absent from the arm. One result differed from Pisani's observations in that neither gas nor fluid interposed between the skin and the focus prevented the tuberculin reaction. In bilateral pulmonary cases, a stronger cutaneous reaction was observed on the side where the lesion was less, the reverse of Pisani's experience. The experiments included cases of cervical lymphadenitis, pleurisy, peritonitis, renal and pulmonary tuberculosis, Pott's disease and coxitis. Human tuberculin (25%) was used by von Pirquet's method.

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**Dependability of Koch's Old Tuberculin Compared with that of Moro's Diagnostic Tuberculin.**

*Leo Meyer, Münch. med. Wchnschr., 68:1286, Oct. 7, 1921.*

Pirquet's reaction has recently been less successful than before the war, often failing where tuberculosis has been diagnosed clinically. This phenomenon is believed to be due to partial anergy of the skin resulting from chronic undernutrition. There is no doubt that the skin, as an organ producing protective substances, plays a part in tuberculosis. The author has sensitized the skin and obtained a vigorous reaction; but it is not certain whether the cutaneous sensitization was due to partial, perhaps even a general, increase of the bodily forces. In any event, it is necessary to determine how far tuberculin may be depended upon to produce the reaction. Moro has recently declared that the antituberculins in use are not dependable and has produced a diagnostic tuberculin (D. T.) by selection of stains and a partial mixture with bovine tuberculin. The author has made comparative tests in 245 children of the value of Koch's old tuberculin and Moro's D. T. and concludes that the latter is superior by far. In tuberculosis recognizable clinically it did not give a much higher percentage of positive reactions, but it gave 23% more of positive results in tuberculosis where the diagnosis was not sure or was made from the subjective evidence. Moro's D. T. is then a specially accurate reagent for the early diagnosis of tuberculosis.

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**Action of Ovarian Products on the Tuberculin Skin Reaction.**

*A. Bouveyron, Compt. rend. Soc. de biol., 85:836, Paris, Nov. 12, 1921.*

The tuberculin reaction in young, tuberculous women was more intense at the menstrual period. The reaction was suppressed or attenuated by fresh graafian-follicle substance of the cow and also by turbid and concentrated glycerin extracts of bovine corpus luteum, entire ovary and of ovary deprived of follicles and corpus luteum. The extracts were obtained by pressure and coarse filtration and contained 1 part of ovarian substance to 2 of glycerin, by weight. These, as well as the follicular liquid, were mixed in the proportion of 0.5 c.c. per drop of crude pasteur tuberculin and used in homogeneous suspension an hour or more after mixture. The congestive halo produced by these substances disappears before the tuberculin reaction fades.

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**Tuberculin Reaction Considerably Increased by Adrenalin; Antagonistic Action of Quinin and Other Substances.**

*A. Bouveyron, Compt. rend. Soc. de biol., 85:834, Paris, Nov. 12, 1921.*

The author studied skin reactions, in tuberculous patients, with tuberculin modified by being mixed with other substances. One drop of the crude tuberculin of the Institut Pasteur was added to 0.5 c.c. physiological salt solution and 0.5 c.c. 1:1000 adrenalin solution. Skin reactions were made symmetrically, on the anterior surface of the shaved thigh, under as nearly the same conditions as possible. An equal quantity of liquid (0.10 c.c.) was used for each test. Several hundred tests show that adrenalin increases considerably the reaction of the skin to tuberculin. The appearance of the reaction is described in detail. Intradermal injections of the tuberculin-adrenalin mixture have the same effect, the resulting reactions being sufficiently violent to injure the skin. In apyretic cases, which showed no reaction, to 1 mg. Calmette tuberculin made every two weeks, the addition of 1 mg. adrenalin produced reaction in about 10 hours. Adrenalin does not appear to form a hypertoxic compound with any portion of the tuberculin. If there be added to the tuberculin-adrenalin mixture 5 cg. of sodium persulphate which stains the adrenalin red, skin reactions result whose average width is about 3 mm., the same dimension appearing with a simple mixture of tuberculin and persulphate. The control reaction with tuberculin alone is about 4 mm. wide, that of the tuberculin-adrenalin mixture about 9 mm. Quinin is an almost perfect physiological antagonist of adrenalin. With one drop of tuberculin plus 0.5 c.c. of a 1 to 5 solution quinin bihydrochlorate, the reaction was much less marked than with control tuberculin. The same effect is produced by 10 cg. of the solution of quinin alone. An aqueous solution of antipyrin (1 to 5) and of pyramidon (1 to 10) produces the same effect as quinin, but less marked.

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**The Isolation of Immune Hemagglutinin.**

*Tanemoto Furuhata, Japan Med. World, 1:1, Tokio, Oct. 15, 1921.*  
Various investigators have attempted to separate pure antibody  
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from serum. Recently, Kosakai treated sensitized blood-cells in sugar solution, and from the antigen-antibody combination recovered five-sixths of the antibody. He believed, however, that an electrolyte medium is necessary. The work here reported was undertaken to secure a purified solution of immune hemagglutinin which could be examined by a direct method, in order that the chemical nature of antibody might be determined. It was attempted to incubate the antigen-antibody complex in a non-electrolyte medium. To obtain the hemagglutinin, a rabbit was immunized with washed hen's blood-corpuses, intravenously injected. Hemagglutinin combines with red blood-corpuses, but the union is with the stroma, not with the hemoglobin. Isolation of pure hemagglutinin was effected by alkali in a non-electrolyte medium. The technic employed was: 2 c.c. of hen's blood-corpuses were washed and sensitized with 5 c.c. immune serum diluted 25 times (titer 1:750), left for half an hour at 37° C. The sensitized blood-cells were centrifuged and washed with 10% saccharose solution. The washed sediments were emulsified in 4.5 c.c. of 10% saccharose solution and 0.5 c.c. of tenth normal NaOH solution, and were incubated at 37° C. for one hour. After centrifugalization, the supernatant fluids were removed as dissociated hemagglutinin, this extract being neutralized with tenth normal HCL. The separated hemagglutinin was purified further by dialysis, by shaking with ether and by concentration in a vacuum, to the required volume. It was determined that hemagglutin can be dissociated from the combination into which it has entered. The ratio of dissociation is greatest in saccharose solution, next greatest in glucose, and less in salt solution. The greatest influencers of alkalis and acids on the separation of hemagglutin are, in the order mentioned, NaOH, H<sub>2</sub>SO<sub>4</sub>, Na<sub>2</sub>CO<sub>3</sub>, and HCL. In salt solution a temperature of 37-50° C. is the most favorable to dissociation of hemagglutinin. In saccharose solution, temperature makes little difference, though a higher seems to be slightly better than a low temperature. Half an hour is enough for incubation. Stroma may be used instead of corpuses, with equal effectiveness. Nitrogen of hemagglutinin dissociated in sugar medium was 0.01541-0.03923 gm. per 100 c.c. and that separated in salt solution was 0.1961-0.04724 gm., while the probable amount of nitrogen obtained by the indirect method was 0.01401 gm. per 100 c.c. The chemical nature of hemagglutinin is being further investigated, but conclusions from the present study are that it is not soluble in ether or in any fat; it does not pass through parchment; the isolated hemagglutinin gives no biuret reaction or any other protein reaction in any marked degree, but gives a positive ninhydrin reaction. It may therefore be inferred that hemagglutinin is a colloidal substance which is closely associated with the protein, but not of the lipin group; nor is it to be considered as belonging to a protein in the usual sense, such as serum protein, though it may contain some nitrogen.

(1e—50)

**Iso-Agglutinins in the Blood of the New-Born.**

*Basil B. Jones, Am. J. Dis. Child., 22:587, Dec., 1921.*

In 1920 Minot and Weld found that by testing both serum and cells it was possible to establish to which of the four groups the blood of newly born infants belonged. Halban was the first to study the  
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relationship of the iso-agglutinating properties of the blood from the new-born to those of the mother's blood. He found that the mother's serum not infrequently agglutinated the infant's corpuscles whereas infant's serum rarely agglutinated the mother's blood. He suggested that the iso-agglutinins did not originate in the mother's blood but in the fetus. Jones has repeated this work and has been able to classify the group in which an infant's blood belonged in 78.7% of 197 specimens. This he ascribed to an improved technic which permits the recognition of weak agglutinins. There is strong evidence that the cells of newly born infants have their full quota of receptors and if this is the case it should be possible to group the blood of newly born infants in 100% of cases. Specimens of infants' serum belonging to Group II definitely agglutinated cells of Groups I and III in 72.8% of cases. The serum of blood in Group III agglutinated cells of Groups I and II in 81.5%. The serum of Group IV agglutinated cells of Group I, II and III in 81.7%. It was determined in Group IV that either iso-agglutinins "a" or "b" or both may be present and in varying proportions. Iso-agglutinins were demonstrated in the serum of a 7 months' fetus. In 14.2% of cases auto-agglutination was observed; 13.7% of the infants' serums hemolyzed washed cells in cover glass preparations at room temperature. These facts indicate the advisability of making the proper tests for compatibility before selecting a donor for transfusion in infants.

(1e-51)

**Observations upon the Conglutation Phenomenon.**

*Frank Maltaner and Elizabeth Johnston, J. Immunol. 6:349, Sept 1921.*

It has been shown that the agglutination of sheep red blood-cells by calf serum is the result of the coagulation of the fibrinogen of the serum. This coagulation is induced by the reaction between the cytozyme in the sheep cell suspension and the other elements necessary for clot formation supplied by the calf serum. The addition of blood-platelets to fresh calf serum produces secondary clots and the fibrinogen-free serum thus obtained no longer agglutinates sheep cells. Calf serum which causes hemolysis of sheep cells no longer reacts after removal of fibrinogen in this manner.

A series of experiments by the authors show a close relation of the agglutinating and hemolytic properties of horse serum and bovine serum, alone and in mixtures, with the elements responsible for the phenomenon of coagulation. The presence of fibrinogen and heat-sensitive constituents of serum is essential for the production of agglutination, hemolysis and the phenomenon of conglutination as observed with these serums and guinea-pig cells. The close association of these phenomena become apparent in the application of technic for re-clotting the serums. In order to remove all of the residual fibrinogen from bovine serum it was usually necessary to add several successive portions of platelets. So long as a clot could still be formed in the serum some agglutination and hemolysis could be obtained, although in a reduced degree.

The agglutination phenomenon described by Bordet was reproduced by using a mixture of inactivated bovine serum and fresh horse serum with washed guinea-pig cells. When the bovine and horse

serums were first depleted of their fibrinogen by secondary coagulation induced by treatment of the active platelets, they no longer gave rise to this "conglutination" phenomenon. Not only the conglutination of guinea-pig blood-cells, but also the hemolysis and the agglutination of these cells by both serums separately or in mixtures, depended upon the presence of fibrinogen and a heat-sensitive serum constituent. The degree of agglutination or hemolysis in the presence of the heat-sensitive serum constituents depends, in part at least, upon the quantity of fibrinogen.

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**Isohemolysins in Human Blood, with Especial Reference to the Blood of the New-Born.**

*Basil B. Jones, Am. J. Dis. Child., 22:598, Dec., 1921.*

The blood of 121 newly born infants and of 144 adults was examined for isoheholysins. These were found in 27.3% of the infant specimens in Group II, III and IV, and in 88.5% of adult specimens in the same groups. Apparently the isoheholysins of adults' serum, as a general rule were stronger than those of infants' serum, though this was not always the case. Isohemolysin "a" which occurs in the serum Groups III and IV is much more frequently present at birth than isoheholysin "b" which occurs in Groups II and IV. This same tendency is also seen in adults' serum, but to a lesser degree. If an excessive amount of red cells which have been twice washed in physiologic salt solution is used for isoheholysin tests, hemolysis will be inhibited. This appears to be due to the presence of antihemolysin in the cell suspension. Even after washing 5 times in normal salt solution antihemolysin is apparently present in the cell suspension.

(1e-53)

**Experimental Intravital Hemolysis. I. The Mechanism of Intravital Hemolysis after the Injection of Hemolytic Immune Serum.**

*R. Bieling and S. Isaac, Ztschr. f. d. ges. exper. Med., 25:1, Berlin, Oct. 14, 1921.*

When erythrocytes of the guinea-pig are mixed in a test-tube with inactivated guinea-pig hemolysin, and fresh guinea-pig serum is added for complement, hemolysis takes place. It was reasonable to assume that hemolysis would occur in the blood-vessels of a guinea-pig inoculated with such hemolysin, through the action of the circulating complement. Gruber has used intravital hemolysis as an argument for the presence of free complement-holding plasma in the entire body. It seems impossible to determine where intravital hemolysis is initiated, and the significance of certain organs in its production.

Intravital hemolysis can be produced in a mouse by injecting it with a mouse-blood-hemolysin produced by the rabbit. The hemolysis of the amboceptor-laden corpuscles in the mouse shows that the complement necessary for hemolysis can be freshly produced in the body of the animal, as mouse blood has no active complement in the serum. This observation makes possible the localization of the hemolysis phenomenon and an understanding of the importance of the several organs in its production. Contrary to Gruber's deductions, hemolysis in the

blood-vessels is much less marked than the destruction of erythrocytes in certain organs, even in animals with complement.

From the results of experiments on mice, intravital hemolysis after the injection of hemolytic amboceptors (specific antibodies) occurs about as follows: (a) The injection of hemolytic serum promptly causes shock and the splanchnic vessels are widely dilated. Shock is the expression of the action between the injected antibody and the antigen (erythrocytes) in the animal body. (b) As part of the shock reaction, there is marked hyperemia of the spleen, which may be enlarged to four times its normal size. This "red tumor" of the spleen is not a characteristic symptom of serum hemolysis, but it furnishes the conditions for the hemolysis which sets in after a definite period of incubation in the wide interstices of the splenic pulp, in which the blood circulates very slowly. (c) The process of dissolution is mainly prepared in the blood-vessels. The injected amboceptor at first circulates in the plasma, but is presently bound by the red cells, leaving the plasma again free of hemolysin. This ends the process in the circulatory system. The binding of the amboceptor alone does not cause hemolysis, as in the test-tube; this applies not only to mouse-serum, which contains no complement, but as well to guinea-pig serum, which is rich in complement. In the blood-vessels the red cells are attacked by the amboceptor, and thereby prepared for lysis. The actual lysis takes place in the organs, primarily in the spleen. (d) To this end, the prepared erythrocytes are carried to the locality where hemolysis is to take place, to the spleen and other organs. (e) The erythrocytes, laden with amboceptor, collects in the spleen where the final reaction between amboceptor and cell takes place. The same functions, which in the test-tube are carried out by fresh guinea-pig serum, are exercised *in vivo* by the red splenic pulp. The hemolysis does not take place in the spleen cells, being neither phagocytosis nor intracellular digestion, but a purely humoral process. (f) As hemolysis occurs in the vascular spaces of the spleen, the organ assumes a dark red to black red color. This second stage, the "black tumor," is characteristic of active hemolysis in the spleen. At the same time the free hemoglobin is reduced to methemoglobin. The spleen at this stage contains a greater amount of free hemoglobin than that found in the circulating blood. (g) Analogous processes in the kidney can be ruled out. They cannot be demonstrated conclusively in the markedly hyperemic liver. In the normal animal the hemolysis takes place mainly in the spleen. Experiments have demonstrated that the liver produces complement, although much less than the spleen which is the main seat for its production. (h) The complement formed in the spleen is secreted into the vascular spaces of its pulp, that is, into the secretory tissue. It is an internal secretion, and is not carried into the circulation but is used up at its source by the hemolysis of homologous erythrocytes. (i) Free hemoglobin and methemoglobin pass into the general circulation from the spleen. They stain the plasma light red, and are excreted by the kidneys. Hemoglobin will enter the circulation, stain the plasma and be excreted by the kidneys only when the amount produced in the spleen is greater than can be taken care of by the organs normally concerned with its decomposition. Since the chief organ for this purpose is the liver, acute hemoglobinuria depends upon the amount of hemolysis and the functional efficiency of the liver.

(1e-54)

**Duality of the Lytic Principles of Bacillus Coli and Staphylococcus.**

*A. Gratia and D. Jaumain, Compt, rend. Soc. de biol., 85:882, Paris, Nov. 12, 1921.*

However identical the phenomena of lysis are for these two bacteria, the lytic principles are different. They differ in sensitiveness to heat and antigenic specificity. Heated above 61° or 62° C. a mixture of the principles loses lytic and inhibitive action for the staphylococcus, but remains effective for bacillus coli up to and over 65° C. Sensitiveness to heat is not absolute, but depends both on the lytic agent and the culture acted upon. It is, therefore, possible that the difference in sensitiveness between bacillus coli and staphylococcus is more apparent than real. Distinction between antigenic properties is marked. Bordet and Ciucă obtained a serum which neutralized the lytic principle of bacillus coli. The authors have prepared a serum which neutralizes the lytic principle of staphylococcus. The two serums neutralize their corresponding lytic principles only; there is no reciprocal neutralization. The specificity and independence of the two lytic principles are thus proved. Lytic principles affecting closely related bacteria may have more or less apparent identity. The differences become apparent if unrelated lytic principles are selected.

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**Research on the Complement Content of Human Blood.**  
*Brinkmann, Cntrlbl. f. Bakteriol., 87:50, Jena, Sept. 1, 1921.*

This research sought to estimate on a sound basis the complement content of the human blood under physiologic and pathologic conditions and to determine whether a reduced complement content is of diagnostic importance. The author relies for this on the addition of an immunizing agent, namely, 0.5 c.c. of a suspension of sheep's red corpuscles, to the serum mixture.

The results of experiments showed that the complement content of the blood of the majority of persons examined, whether sick or well, was about the same, an average of from 0.08 to 0.1. In a few exceptions however, the serum had an abnormally low complement content. The latter should not, however, be regarded as of diagnostic importance, as it is frequently met in perfectly healthy subjects. The complement content of serum is much more stable than is popularly believed. The author also found that serum preserved for fourteen days still gave the complement reaction.

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**Complementing Activity of the Blood-Serum with Relation to Adrenal Deficiency.**

*Enrique E. Ecker and J. M. Rogoff, J. Immunol., 6:355, Sept., 1921.*

A fair proportion of rabbits survive complete bilateral adrenalectomy. It has been assumed that this might be accounted for by the presence of accessory adrenal tissue. Accessory glands when present in the rabbit are usually situated along the cava or near the vessels of the kidney and can generally be detected readily and removed during the operation. Such accessory adrenals consist only of cortical sub-

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stance, and chemical and microscopic examinations fail to disclose the presence of chromaffin material. When accessory adrenal tissue is present the amount is much less than the fraction of adrenal which is generally found necessary to sustain life. Five rabbits were used in the experiments, and a sixth was used as a control. The complement titers of these animals show that comparatively small variations occur following the operation and also in the control animals, indicating that the absence of the adrenal glands has no demonstrable influence on complement activity. The anti-sheep hemolytic system was used throughout in the experiments.

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**Photolability of Complement.**

*E. G. Lundberg, Compt. rend. Soc. de biol., 85:758, Paris, Oct. 22, 1921.*

Complement employed was that of swine serum, the technic that for titration of hemolysis adopted by the Institute of Serotherapy of Denmark. The first series of tests concern the attenuation of the complement by light. The speed of the reaction may be expressed by the law of monomolecular reactions. Dependence of rapidity of attenuation on the temperature is slight, almost no difference existing for temperatures between 26° and 46°. Speed of the reaction is modified in proportion to the intensity of light; it is increased also as the attenuation is augmented. In the course of exposure to the light, the serum changes from an orange to deep yellow color, with increasing opalescence.

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**Artificial Complement.**

*L. von Liebermann, Deutsch. med. Wchnschr., 47:1283, Berlin, Oct. 27, 1921.*

Some 14 years ago, it was stated that the complement in immuno-hemolysis is specifically connected with the soap-like substances normally present in blood-serum. The author has experimented with suitable mixtures with the object of disproving this hypothesis. His mixtures consisted of solutions of sodium oleate and chlorid of lime in chemically pure methyl alcohol, in conjunction with serum derived from rabbit's blood. The first results showed that the artificial complement is just as effective in activating hemolytic immune-bodies as natural complement. The artificial complement also proved as effective with guinea-pig serum. In numerous cases of tuberculosis, the artificial complement gave results agreeing with those obtained by the natural complement.

The author regards the question whether the artificial complement can be specifically combined through the medium of an antigenic mixture, as solved in the affirmative.

The artificial complement is not, as yet, available for use in practice.

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**Quantitative Relations between Amboceptor and the Serum of Complement-Deficient Guinea-Pigs.**

*Enrique E. Ecker, J. Infect. Dis., 29:611, Dec., 1921.*

The author studied the serums of a strain of guinea-pigs known (Sec. 1—Page 154)

to be deficient in complement, and confirmed their great deficiency, as previously noted by Downing and Moore. The deficient action has been shown not to be due to amboceptor interference, since the increase of amboceptor leads to hemolysis of the cells. These serums when employed in comparatively small doses (0.1 c.c.) and in the presence of 500 units of hemolysin readily cause lysis. The deficient serums react in a similar manner as cobra venom inactive serums, in that the addition of normal inactive homologous or heterologous serums markedly enhances hemolysis, this observation confirming the results of Coca. It was found that various inactive serums have varying degrees of activating power when added to the deficient serum amboceptor cell mixture, a phenomenon similar to that observed by Jonas in the case of cobra venom inactivated serum. By the increase of amboceptor and the addition of normal, inactive, homologous or heterologous serums, the deficient serum has been made to act within the usual lytic range of normal guinea-pig serum.

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**Ferments of Human and Animal Blood in Narcosis and Certain Poisonings.**

*John Grönberg, Finska läk.-sällsk. handl., 63:429, Helsingfors, Sept.-Oct., 1921.*

Abderhalden was the first to discover that when a foreign protein, fat or carbohydrate is injected into the circulation, ferments which are able to digest the material injected appear in the circulation. On the basis of these experimental observations, he claimed that the introduction into the organism of such foreign substances as medicaments or toxic material does not injure the organism because certain ferments circulating in the blood protect the organism. The author has studied this theory and observed the effect of various forms of narcosis and poisonings on the ferments of human and animal blood. He observed that almost all serum from human beings and animals which had been affected by ether, chloroform, carbolic acid, lysol, veronal, morphin or lead-containing substances, contains such protective ferments as Abderhalden has claimed. Under the effects of ether, serum and lung reactions when tested are more frequently positive than under the influence of chloroform. In cases of acute poisoning due to carbolic acid or to lysol, the substratum of the liver and kidneys is especially affected. The serum from individuals with veronal poisoning does not affect the kidney. The serum from poisoning due to chronic morphinism or to lead almost always affects the substratum of the kidney. The serum of a morphin addict reacts positively to thyroidin. The serum of all experimental individuals always revealed a negative Abderhalden reaction on the part of the tested substrata before narcosis due to ether or chloroform, but the reaction was always positive during the narcosis. The serum from individuals with acute or chronic poisoning gave a positive reaction on the part of certain substrata, while the simultaneously examined control serum from normal individuals reacted negatively when tested with the same substrata.

The author comes to the conclusion that various substances of pronounced toxicity produce, in the human and animal blood, ferments

which it does not contain under normal conditions. He believes that his experiments have confirmed Abderhalden's theory concerning the existence of protective ferments in the blood.

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**Bacillus Pyocyanoides and the Antiprotease Reaction.**

*A. Falque, Compt. rend. Soc. de biol., 85:799, Paris, Nov. 5, 1921.*

Specific substances obtained by the injection into rabbits of a filtrate from cultures of proteolytic bacteria, and the action of the proteases of *Bacillus pyocyanus*, have suggested that the antiprotease reaction may serve to identify proteolytic bacteria. In addition to the usual pyocyanic bacilli, which produce typical colorations, Gessard has also studied a class which he calls pyocyanoid bacilli. The latter are not typically chromogenic, but they respond to pyocyanic antiprotease tests. Various specimens were studied; they were derived from cultures of *pyocyanus* which had degenerated of which were obtained from various suppurations. The only traces of the original characters still remaining were the form of the culture, the aromatic odor, and a vague fluorescence in bouillon; the antiprotease reaction determined their classification as a species of *pyocyanus*. The reaction is very sensitive and serves to show whether or not a given bacterium is proteolytic.

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**The Proteolytic Serum Ferment.**

*Richard Stephan and Erna Wohl, Ztschr. f. d. ges. exper. Med. 24:391, Berlin, Sept. 22, 1921.*

Abderhalden's theory of specific protective ferments is based upon the assumption that the serum, physiologically, contains no proteolytic ferment, and that every fermentative proteolysis depends upon the parenteral ingestion of albuminous substances foreign to the blood. This foundation of Abderhalden's theory has been shown, by Oller and Stephan, to be unjustifiable. The latter have proven that tryptic ferments are present in every serum. However, their work does not show that the formation of albumin decomposition products is really due to fermentative splitting of the substances added to the serum, such as placenta, or carcinomatous tissue, and not to autolytic splitting of the serum albumin. That the latter takes place is proven by Plaut, who demonstrated ninhydrin-reacting substances in experiments in dialysis, after the addition of colloidal substances like kaolin, instead of coagulated tissue substances. It must now be proved that fermentative splitting of the albumin occurs in coagulated tissue substances. The process is never microscopically visible, even when large quantities of serum are employed. On the contrary, sterile serum is an ideal preserving-fluid for heated tissue substances. It is also a fact that active serum, supposed to have a proteolytic effect on various tissues, powerfully inhibits, and even completely abolishes, the effects of trypsin solutions. The usual casein-trypsin test is valueless for showing the antitryptic power of the serum. It is evident that the strongly inhibitive effect of the serum on trypsin digestion is immediately inactivated by heating to 56° C. But it also appears that the difference between active and inactive serum is only apparent, because of changes in the precipitability of casein. If, after the addition of the various serum

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dilutions to the casein-trypsin mixture, 2 drops of dilute acetic acid are also added, serum inactivated by heating to 56° C.—even in dilutions of 1 to 2 drops per 10 c.c. of the solution—will completely prevent the acetic acid precipitate. Active serum in no concentration affects the precipitating power of acetic acid. The casein-trypsin method is thus of no value for showing the difference in the antitryptic inhibitive effects of active and inactivated serum. (The addition of acetic acid and serum to a casein-trypsin mixture distinguishes active from inactivated serum).

For the study of the antitryptic action of serum, the authors used fine fibers of carmin-fibrin. They found that trypsin digestion of the fibrin was inhibited in all cases by active serum, but was not inhibited by serum heated for one-half hour at 56° C. It follows that the antitryptic action of the serum is not determined by products of albumin catabolism. A series of tests was tried in which, as in heat inactivation, the inhibitory effect against fermentative proteolysis was destroyed, without destroying the effectiveness of any proteolytic ferment which might be present in the serum, as occurs after heating. For demonstrating such a proteolytic ferment in the serum, an albuminous substance must be selected which is readily acted upon, and which, also, in the presence of small quantities of ferment, will reveal macroscopically visible changes in tryptic digestion. Carmin-fibrin is such a substance. It was used in very fine fibers from 2 to 3 mm. long. Each fiber was placed in a Wassermann tube with a trypsin solution and with various quantities of serum, and was kept at 37° C. Digestion was indicated by the disappearance of the fibrin in twelve, twenty-four, thirty-six and forty-eight hours.

It was found in more than 100 tests that active serum of various origins had no proteolytic effect on the fibrin. On the other hand, serum inactivated by a temperature of 56° C. fully digested the fibrin in dilutions of 0.8 serum plus 0.2 NaCl solution to 0.3 serum plus 0.7 NaCl. The fibrin was not digested by solutions stronger or weaker than these. Thus inactivation of the serum destroyed its colloidal, inhibitive action and permitted the proteolytic ferment action free play according to the degree to which it was affected by the heating. After many trials, it was found possible to secure inactivation which only arrested the colloidal, inhibitive effect, leaving the fermentative action unaffected, thus proving the presence of a proteolytic ferment in the serum. The method consists in adding 10 drops of chloroform to 5 c.c. serum, shaking for from one to two minutes, allowing the chloroform to settle and then pipetting off the supernatant mixture; from the latter, the chloroform is evacuated for ten minutes until the fluid is again entirely clear; a small quantity of chloroform remaining in the serum, causes no difficulty. In some cases, proteolysis occurs after the use of chloroform in 65% of the cases. Treatment of the serum with acetone and clay, animal charcoal, and inulin, with subsequent centrifugization, or treatment by active agitation or dialysis, gave the same result as that obtained by chloroform treatment, but the action was not nearly so uniform.

Dialysis was the next most effective method after chloroform. The inhibitive effect of normal serum being thus removed by the chloroform, and proteolytic fermentation being thus rendered visible, it seemed probable that the ferment was present in normal, active serum, being

merely inhibited. It seems much less probable that active ferment is not present in untreated serum, and that activation of the ferment is due to the treatment. This appears even more improbable when one considers the various, purely mechanical processes which have the same effect as the chloroform treatment, although their action is not so uniform.

The authors believe, although absolute proof is lacking, that the physicochemical structure of the serum protects it absolutely against sero-autolysis, at least as regards highly molecular proteins. If the structure of the serum is changed by mechanical action, this protection may be lost, and the preformed, proteolytic ferment may become active. All processes which break through the protection against autolysis invariably produce faint clouding of the serum; this fact suggests that labilizing of the serum-globulin is related to the appearance of proteolysis. Therefore all processes which produce fibrinolysis in serum simultaneously inhibit the complement effect of the serum in hemolytic experiments. Although chloroform inactivation demonstrates the presence of a proteolytic ferment in the serum in two-thirds of the cases, this fact does not explain all the conditions. The ferment is apparently always present, and only a more effective method of inactivation is needed to prove its presence. Since chloroform appears to injure the ferment, and also since unknown factors are concerned, quantitative determination of the proteolytic serum ferment is valueless. The demonstration of a proteolytic serum ferment existing in the majority of normal individuals is a strong argument against Abderhalden's theory of protective ferments. It is conceivable that these specific ferments exist side by side with the non-specific ferments generally present. But there is no proof of this, while there is no doubt that the original substrates markedly altered by heating, are acted upon by the non-specific ferments. It may be assumed that a large proportion of the ninhydrin-reacting substances found by dialysis are due to non-specific proteolysis. All serum-ferment experiments should be repeated systematically on the basis of the authors' findings.

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**Proteolytic Ferment and Coagulation Ferment.**

*Richard Stephan, Ztschr. f. d. ges. exper. Med., 24:407, Berlin, Sept. 22, 1921.*

Parallel to previous observations on the presence of a proteolytic ferment in the serum, experiments were made on coagulation to complete Klinger's studies. Previous experiments had shown that a ferment is necessary for extravascular coagulation. This ferment, believed to be specific, is formed in the cells of the reticular or splenic system and is given off into the blood. Augmented function of the reticular cells increases the coagulation ferment in the blood. In the case of all patients in whom the hemolytic activity of the splenic system is heightened, ferment formation is also increased; it may therefore be said that increased function of the splenic system affects all functions of the cells concerned. However, certain studies indicated that the coagulation ferment was not specific and that a general non-specific proteolytic ferment produces all fermentative splitting of albumin. The author found: (1) In croupous pneumonia there is always an increase of coagulation ferment before the crisis. (2) There are considerable

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variations in the individual coagulation time and ferment titer in the course of the day. These are highest during digestion, especially after a meal rich in albumin. In order to reveal the identity of serum ferment and coagulation ferment, the coagulation ferment in every serum was determined by "coagulation analysis," the proteolytic ferment by the carmin-fibrin method. (3) Tests were made to determine whether or not shaking active serum with chloroform caused a quantitative change in the coagulation ferment in the blood. (4) The effect of radiologic stimulation of the spleen on serum protease was studied. (5) The two ferments were compared in the blood of patients showing increased or decreased ferments.

The determination of serum protease by the fibrin method has been previously described. The method for the coagulation ferment was given in the *Deutsch. med. Wchnschr.*, 1920, No. 25. The fermentative power of the serum is estimated by the "coagulation-accelerating factor," i. e., the number resulting from division of the coagulation time of normal blood by the coagulation time produced by adding 0.05 c.c. active serum to 20 drops normal blood. Normally, this quotient or factor is about 1.5 provided blood freshly taken from the vein of a normal donor is used for the determination. It is not always easy to find such a donor. Neither the fibrin method nor the coagulation analysis furnishes an absolutely reliable value, but relative values obtained from normal individuals may be compared. Experiments showed that coagulation ferment and tryptic serum were parallel in quantity, and that increase or decrease in the concentration of one was accompanied by a like change in the other. Stimulation of the spleen always produced increased concentration of both ferments, which proves that they have a common origin. By shaking serum with chloroform, which brought the fibrinolytic ferment of the serum into evidence, the activity of the coagulation ferment was increased.

In hemolytic icterus, pernicious anemia, endocarditis lenta, and after serious loss of blood, the concentration of the two ferments increases to the same degree. Lessening of both occurs in exhaustion, carcinomatous cachexia, polycythemia rubra and idiopathic high pressure. The action of the two ferments, therefore, seems to be identical, although there is no real proof of the identity. The determination of ferment concentration is significant in diagnosis. It is increased in pernicious anemia. After extirpation of the spleen in pernicious anemia, the ferment content becomes normal, and increases again with the renewed progress of the anemia, when the remaining reticular system has taken over the function of the spleen. The determination is also prognostic, since it indicates the protective power of the body. Finally, increase or decrease of all proteolytic processes may be affected therapeutically by roentgenologic stimulation of the spleen.

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**The Defensive Reactions of Animals Infected with Spirochæta Pallida.**

*Wade H. Brown and Louise Pearce, J.A.M.A., 77:1619, Nov. 19, 1921.*

By inoculation of rabbits with *Spirochæta pallida* one may obtain an infection which progresses no further than the production of  
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a lesion at the site of inoculation; or a variety of conditions may occur, and infection may take place without the production of a lesion at the portal of entry, with no clinical evidence of an infection.

The 3 conditions of peculiar significance are latency, relapse, and progression of the disease. A rabbit once infected with *Spirochæta pallida* harbors virulent organisms for the remainder of its life, yet active manifestations of the disease may be difficult to detect and are rarely observed after the first few months of infection. The prime object in the defensive reaction is repair of the harmful effects, and secondly the inhibition of the growth of spirochetes so that the infection is brought under control. Relapse is prone to occur, and it can be shown experimentally that the resistance acquired is definitely related to the extent or severity of the injury produced. The resistance may be transient or relatively enduring, but tends to increase as infection progresses until it is sufficient to afford a safe margin of protection against the organism. Among the conditions affecting the evolution of the disease, there are 2 which appear to be definite laws: "the law of inverse proportions," and "the law of progression or sequence".

The animal organism must be regarded as possessing definitely organized lines of defense which operate in accordance with certain general principles or laws. The manifestations of disease depend not only on general laws governing syphilitic reactions, but on any and all conditions affecting the initiation of the infection, the resistance of the host or the pathogenic properties of the organisms themselves.

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**Studies on Complement Fixation. II. The Velocity of Fixation of Complement in the Wassermann Test.**

*R. L. Kahn and R. M. Olin, Jr., J. Infect. Dis., 29:630, Dec., 1921.*

There exists a great difference of opinion with regard to the time and temperature of fixation of complement in the Wassermann test, different workers recommending 30, 40, or 60 minutes in the water-bath, 2 hours in the icebox, plus 30 minutes in the water-bath, or 4, 8, 10, or 12 hours in the icebox. The authors carried out complement fixation tests with a sheep-cell system, using 2 units of complement, 2 of amboceptor, and 4 to 5 of antigen. Six antigens were employed. The periods of fixation were 0, 5, 15 and 30 minutes and 1, 2, 3, 4, 5, 6 and frequently 7 hours. The temperatures of fixation were water-bath, room, and icebox, and in some cases, water-bath and icebox.

It was observed that the velocity of fixation of complement is not markedly affected by temperatures ranging between water-bath and icebox. The tendency for slightly stronger fixation at icebox temperature compared with that of the water-bath was noted with all antigens, except the Noguchi. The latter antigen showed a tendency for somewhat stronger fixation at water-bath temperature. It was also observed that a fixation period of four hours at icebox temperature approaches the maximum amount of fixation of complement with all antigens, including the Noguchi, although the latter in a few cases showed slightly more fixation after one hour in the water-bath than after four hours in the icebox. Finally, it was shown that the velocity of fixation of complement is directly proportional to the concentration of antibodies in the syphilitic serums.

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(1e-66)

**Studies on Complement Fixation. III. The Effect of Heat on Complement-Fixing Antibodies.**

*R. L. Kahn, S. R. Johnson and A. G. Boyd, J. Infect. Dis., 29:639, Dec., 1921.*

The authors studied the effect of heat on three types of complement-fixing substances: those present in syphilitic serum, those present in rabbits immunized with purified proteins, and those found in animals as a result of bacterial immunization. It was found that thermal destruction of syphilitic complement-fixing substances is markedly influenced by the mode of fixation. When fixation was carried out for one hour at water-bath temperature, the heating of serum for thirty minutes at 56° C. caused, in a total of 87 serums tested, an average antibody destruction of 32%. When fixation was carried out for four hours at icebox-temperature, some serums showed a slight loss, others no loss, and still others a considerable gain in antibody content, with the result that the average finding of the 87 serums tested represented a gain of 10%. Heating syphilitic serums for twenty minutes at 62° C. gave an average of 75% antibody destruction with water-bath fixation, and 46% with icebox fixation.

The type of antigen employed was also found to influence thermal destruction of these antibodies. Heating serums for thirty minutes at 56° C. caused either little antibody destruction or an apparent gain in antibody content, with 2 alcoholic extract antigens and 1 cholesterinized antigen and icebox fixation, while even with this mode of fixation considerable destruction was noted with the Noguchi antigen at this temperature and period.

Finally, it was found that complement-fixing antibodies obtained on protein or bacterial injections were comparatively thermostable. These antibodies were found to be capable of withstanding a temperature of 65° C. Temperatures of 70° C. and 75° C. showed varying degrees of antibody destruction, somewhat more so in the case of bacterial immune bodies than of those obtained on protein injections. With regard to the effect of the mode of fixation on specific antibody destruction due to heating, no marked difference was observed between water-bath and icebox temperatures.

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**Studies on Complement Fixation. IV. On the Affinity of Sheep Corpuscles for Antisheep Hemolysin.**

*R. L. Kahn and D. S. Lyon, J. Infect. Dis., 29:651, Dec., 1921.*

A quantitative study of factors governing the affinity of sheep corpuscles for antisheep hemolysin was carried out. The hemolysin was obtained by immunizing rabbits with sheep corpuscles in the usual manner, and the corpuscles interchangeable from 5 different sheep. A unit of hemolysin was taken to be the smallest quantity which completely hemolyzed 0.1 c.c. of a 5% suspension of sheep cells in the presence of 0.1 c.c. of pooled guinea-pig complement after 15 minutes' incubation in the water-bath. In the first series of experiments, the rate of absorption of antisheep hemolysin by sheep corpuscles at different temperatures was studied, the extraction periods being 5, 10, 15, and 20 minutes, and the temperatures, water-bath, room, and icebox; the hemolysin is extracted from both salt and pooled serum solu-

(1e-67)

tions. When 0.05 c.c. quantities of packed sheep corpuscles were added to 1 c.c. quantities of either salt or serum solutions, each containing 400 units of hemolysin, the differences in the quantity of hemolysin absorbed at extraction periods of 5 to 20 minutes were not marked; neither were there large differences in the number of units absorbed at water-bath and icebox temperatures.

In the second series, the effect of the concentration of hemolysin on the absorption capacity of 0.05 c.c. of packed sheep cells was studied, the extraction in each case being carried out for 10 minutes at room-temperature. The number of hemolysin units that this quantity of sheep corpuscles is capable of absorbing was found to be directly proportional to the concentration of hemolysin. The largest number of units absorbed by 0.05 c.c. of packed cells in these experiments was 18,000, which does not, however, represent the true absorption capacity of this quantity of sheep cells. The hemolysin serums employed, either undiluted or in low dilution, contained in every instance large numbers of hemagglutinins, which tended to bring about immediate precipitation of the corpuscles, and thereby prevented proper contact between the hemolysin and the cells.

Finally, the effect of time and temperature on the hemolysin absorption capacity of 0.05 c.c. of packed sheep cells was studied. It was found that a ten-minute extraction period at room-temperature was in most cases equivalent to a one-hour or two-hour extraction period at water-bath temperature. In a few cases there was less extraction after one hour or two hours in the water-bath than after ten minutes at room-temperature. This is believed to be due to dissociation of hemolysin and cells after prolonged extraction at 37.5° C., and also to the hemolysis of some corpuscles at this temperature with the liberation of hemolysin.

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#### Researches on the Wassermann Test.

*Carlo Martelli, Riforma med., 37:1099, Naples, Nov. 19, 1921.*

Everyone who has seriously undertaken the serum-diagnosis of syphilis has complained that his results do not correspond with those of others equally conscientious. Four points are to be considered: (1) Disparity of reaction; this is based apparently on different properties of the lipoids and globulins that give the colloidal reaction between serums and antigens. These differences are less in fresh syphilis and reach their maximum in the last stages of the disease. The difficulty can easily be overcome by treating the serum with several antigens and taking the average reaction. (2) Specificity; the Wassermann reaction is specific for syphilis both active and reactivated. The facts that several antigens having nothing in common with treponema and that syphilitic organs can react in presence of the serum, show that the physicochemical combination to which the deviation of complement is bound in the Wassermann reaction has nothing strictly specific about it. The union of emulsion of special lipoids with syphilitic serums shows a special colloidal state capable of demonstration with flocculation or deviation of complement. It is therefore not remarkable that such colloidal disturbance can be induced by other diseased conditions than syphilis. Hence the quantity of flocculation and deviation of complement, that are induced within given limits of time

is more to be considered than to the quality. (3) The maximum of reaction is given only by syphilitic serums in a state of activity. This is shown clearly in a table. A strong arrest of hemolysis in the presence of 4 or 5 different antigens is a sure proof of specificity for syphilis; weak or partial ones are proof of other diseases. Serums surely syphilitic can give strong reactions even with weak dosage of antigens, (0.01-0.02) the usual dose of 0.10 and 0.20 is ample. But in doubtful cases, 0.40-0.50 should be used, which may give a clearly positive reaction. (4) The method of biologic reactivation is of enormous scientific value for diagnosis. A table shows the largest percentage from arsenobenzol endovenously; other means are calomel and biniodate of mercury. In the period of latency, a brief treatment with any one of these will usually start the formation of antibodies. The persistence of a negative Wassermann in a reactivated serum, if clinical signs are lacking, has an absolute value for the rejection of a diagnosis of syphilis.

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**Studies in the Standardization of the Wassermann Reaction.  
XXI. A Study of the Methods of Conducting the Secondary Incubation and Time of Reading of Complement Fixation Reactions in Syphilis.**

*John A. Kolmer, Am. J. Syph., 5:614, Oct., 1921.*

The kind and temperature of the incubator employed for the secondary incubation in complement fixation tests has an important influence on the reaction. Water-bath incubation at 37° C. facilitates hemolysis better than an air incubator at the same temperature, but air incubation occasionally results in stronger reactions due in part to the time allowed for the fixation of complement by syphilitic serum and tissue extracts before hemolysis occurs. Secondary incubation in a water-bath at 30° C. occasionally yields stronger reactions than at 40° C., but the lower temperatures may result in incomplete hemolysis of the controls; the optimum temperature for a water-bath is 35°-38° C., with an average of 37° C.

With a primary incubation of 18 hours at 8° C., warming the tubes in a water-bath at 37° C. for from five to fifteen minutes (not longer) before the addition of hemolysin and corpuscles occasionally results in stronger reactions than when hemolysin and cells are added in the cold tubes. A longer period of warming is frequently unsatisfactory due to the increased nonspecific fixation of complement by serum or tissue extract. With the antisheep and anti-ox hemolytic systems the most delicate reactions are observed when the results with each serum are read immediately after complete hemolysis of the antigen, hemolytic and individual serum controls. Next in order of sensitiveness are reactions read immediately after an arbitrary period of secondary incubation of one hour. An arbitrary period of secondary incubation followed by placing the tubes in a refrigerator overnight before reading the reactions, occasionally results in weaker reactions and even falsely negative reactions with weakly positive serums unless special precautions are taken as described in another contribution, abstracted in this issue.

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**Studies in the Standardization of the Wassermann Reaction.  
XXII. A Method of Preventing the Influence of Natural Anti-sheep Hemolysin upon the Complement Fixation Reactions after the Secondary Incubation.**

*John A. Kolmer, Am. J. Syph., 5:628, Oct., 1921.*

The influence upon complement fixation reactions after the secondary incubation of an excess of antisheep hemolysis represented by natural hemolysis in human serum may be prevented by heating the tubes in a water-bath at 55° C. for ten minutes. This method of heating prevents further hemolysis by the destruction of complement which thereby breaks up the hemolytic system. Heating in a water-bath at 55° C. for ten minutes does not cause the hemolysis of sheep cells. The reactions observed after heating the tubes for ten minutes at 55° C. after the secondary incubation followed by settling in a refrigerator until the next day are practically identical with the reactions immediately after the secondary period of incubation.

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**Ether and the Wassermann Reaction.**

*J. Forssman, Compt. rend. Soc. de biol., 85:828, Paris, Nov. 5, 1921.*

The results with serums supposedly freed entirely from ether by evaporation have not been uniform. There is no proof that ether is totally eliminated from mixtures with serum or similar substances, except that afforded by the absence of odor which is an insufficient guide. Traces of ether persist, and on inactivation at 56° of a positive solution, these traces change the reaction from positive to negative. This sensitiveness to ether explains discrepancies in the results of reactions. If traces of ether are completely removed by evaporating in vacuo at 30° before inactivation, the solution remains positive. If, after ether extraction, new ether is added and evaporated in vacuo at 30°, after inactivation, the solution is positive because all ether was removed before inactivation. The composition of serums is very variable, but the quantity of ether used is immaterial. Variations are due to traces of ether. Its effect on the Wassermann reaction, alike for serums and positive solutions, may be due to modifications of dispersion rather than to destruction of any particular substance.

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**The Proportion of Antibodies in the Wassermann Reaction.**

*Pier Francesco Zuccola, Policlinico (Pract. Sect.), 28:1463, Rome, Oct. 31, 1921.*

An improved method has lately been tried by Dujardin and Peyre for the estimation of the degree of positiveness of the Wassermann reaction. It consists in determining in any given serum the dilution-limit containing a sufficient quantity of antibodies for the constitution of the fixative complex. The liquid under examination is diluted to 10% and 1% or even 0.1% when necessary. Drops are used instead of cubic centimeters, in droppers giving 0.05-0.1 c.c. per drop. Tables show the results for 8 different dilutions. A result is considered positive in any tube in which hemolysis is found incomplete. If this is the case in the first tube (dilution 1:10) the liquid contains 1 antibody unit (called (Sec. 1—Page 164)

sigma); if incomplete in the first four (up to 1:100), the liquid contains 10 units. If it is positive at a 1:40 dilution, and not at 1:100, the 1:10 dilution base (1:10) then contains:  $\frac{1}{10} = 4$  antibody units. Experi-  
1:40

ments have been made prolonging these researches with fractions of cubic centimeters of a 1:10 serum solution; no matter how intense the reaction, it does not go beyond the said limit in the dilution. While this method neither simplifies nor expedites the test, it offers a precision that makes it advantageous over those methods in use today, especially in the observation of the reactive processes in the clinical evolution of the lesion.

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**A Preliminary Report on a Method of Determining the Number of Complement Binding Units in Sera Giving Positive Wassermann Reactions.**

*Archibald McNeil, J. Lab. & Clin. Med., 7:109, Nov., 1921.*

As many serums contain more than enough complement-binding units to give a 4-plus reaction the clinician should be able to estimate the number of complement-binding units in any serum. In cases with a large number of complement units the reaction may be 4-plus for a long time after treatment is begun, and with 4-plus as a standard the treatment does not show whether improvement is actually taking place, knowledge of which would be of value to physician and patient. McNeil describes a method for determining the complement-binding units, using 0.1 c.c. of serum—that is the amount which in the classical Wassermann test gives 4-plus—as a starting point and making a series of dilutions each of which will differ from the succeeding dilution by exactly 1-plus.

For an unknown serum a preliminary titration must be made, using 1:10 and 1:100 dilutions, by the same technic as in amboceptor titration, with 0.1 c.c. antigen and 1.0 c.c. complement as standardized for the regular test, with the proper antigen and serum controls. This gives a rough estimate of the number of complement-binding units present. After shaking, the tubes are put in the ice-box for four hours to bind complement. Then they receive 2.0 c.c. of sensitized sheep's cells and remain in a water-bath at 37° C. for fifteen minutes after antigen and serum controls show complete hemolysis. They are returned to the ice-box and are read at the end of twelve hours. The reading is made on the tube that shows least inhibition of hemolysis. For example, if a tube containing 0.4 c.c. of a 1:5 dilution of serum shows complete inhibition of hemolysis and the tube containing 0.4 c.c. of a 1:6 dilution of serum shows slight hemolysis the reading will be 5-plus. The after-time in the ice-box is necessary to prevent variations in the readings of a series of titrations on the same serum with different hemolytic systems. The best results have been obtained by using a dilution of amboceptor containing 5 Bordet units in 1 c.c. Complement diluted 1:30 is titrated against 2 c.c. of sensitized sheep's cells, read after thirty minutes in the water-bath, and the dilution of complement is so adjusted that 1 c.c. will contain 2 units of complement. Antigen is used in the same amount and dilution as in the routine Wassermann tests, the same antigen in a constant dilution throughout a given series of titrations.

Further experiments are to be reported on "Wassermann fast" cases which are regarded as cases in which perhaps the treponemas have become immune to one or more drugs. Experiments are under way to test this hypothesis and to see whether this method can be used to show when a change of treatment is indicated.

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**The Bordet-Wassermann Reaction and Flocculation.**

*M. Rubinstein, Paris méd., 11:377, Nov. 12, 1921.*

Even early in the history of the Wassermann test the first stage of the reaction was considered a flocculation or precipitation reaction. Numerous experiments have proved that this conception is correct and several processes of flocculation have been proposed. However, the hemolysis reaction and the flocculation phenomenon have the same significance, and preference is given to one or the other merely on the basis of personal taste, although flocculation is hard to see and difficult to interpret.

A number of new procedures have been proposed for the sero-diagnosis of syphilis, but they do not differ essentially from the old Bordet-Wassermann reaction. All are based upon the mixing of the patient's blood heated for 20-30 minutes at 56°, an organ extract (liver or heart) and guinea-pig serum, which supplies the complement. For a long time attempts have been made to obtain a quantitative reaction. For this purpose the minimum dose of human serum or organ extract, or the maximum dose of complement which gives a positive reaction are ascertained. Colorimetric scales have also been proposed to determine the strength of positive reactions. Methods based on the use of heated serum are subject to error. A weak positive reaction is often erroneous and unless checked by other methods the results express more the personal interpretation of the experimenter than the actual condition of the disease.

Direct flocculation methods are based on the use of various preparations, including the same organ extracts used in the Wassermann reaction, and such substances as sodium glycocholate and cholesterin with the addition of a serum containing alexins. The Sachs-Georgi method is considered by many as the most successful attempt to replace the hemolytic method by direct flocculation. It consists in the addition to heated serum of cholesterinized beef-heart extract, the intensity of flocculation being measured by means of an agglutinoscope. The various processes of direct flocculation have a theoretic interest but should only be used in conjunction with the Wassermann reaction.

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**The Serum Reaction of Syphilis. Photometric Measurement of Flocculation Based on Its Weight.**

*Arthur Verne, Presse méd., 29:957, Paris, Dec. 3, 1921.*

The author's serum reaction is based on the use of suspensions of certain finely divided substances ("granulifere") which in contact with normal human serum give rise to flocculation. When various dilutions of serum are tried with the same dose of granulifere, it is seen that flocculation varies in intensity from zero to complete flocculation. From these results a curve may be plotted out. The serum of syphilitic  
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patients possesses the property of definitely modifying this curve. The test is simplified by studying the dilution which gives a maximum precipitate with a syphilitic serum and no precipitate at all in the case of a normal serum. Under these conditions the degree of syphilitic flocculation has been shown to increase or diminish with the intensity of the infection. In order, therefore, to estimate the latter it is necessary to measure this flocculation accurately. For this purpose the author has devised an apparatus which gives two fields of light of equal intensity. If a liquid containing a precipitate in suspension is interposed before one of these, the light is absorbed to a degree corresponding to the weight of the precipitate and the field appears darker. By means of a device the intensity of the other field may be reduced so as to match the first. The weight of the precipitate may then be read off on a graduated standardized scale connected with the device.

This method is simpler and more accurate than the colorimetric process previously used by the writer, which permitted the estimation of flocculation only within certain rather narrow limits, while with this process all degrees of flocculation may be measured.

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**The Estimation of Meinicke's Third Modification.**

*F. von Guifeld, Deutsch. med. Wochenschr., 47:1295, Berlin, Oct. 27, 1921.*

The Wassermann reaction and Meinicke's third modification agree in 94.9% of cases. The best method of controlling self-flocculating serums is by using absolute alcohol prepared in the same manner as the alcoholic extract. The mixture is made up of 1 part absolute alcohol, to which is immediately added  $\frac{1}{2}$  part of distilled water. After standing for one hour, 7 parts of a 2% solution of sodium chlorid is added. The mixture contains 11.8% alcohol and about 1.65% of sodium chlorid. Of 1,500 determinations with this controlling compound, "self-flocculation" was evident in 31, or about 2%.

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**Sachs-Georgi and Meinicke Reactions in the Serodiagnosis of Syphilis.**

*Giuseppe Vercellana, Gior. di clin. med., 2:534, Parma, Sept. 20, 1921.*

The Sachs-Georgi reaction (cholesterinized antigen), contrary to the assertions of some enthusiasts, cannot be entirely substituted for the Wassermann reaction. It has been found rather inconstant and tends to give positive results in clearly nonsyphilitic individuals. In soft chancre the Sachs-Georgi reaction was positive in 11 of 42 cases, when both the original Wassermann and the Meinicke salt modification were negative. With cerebrospinal fluids the Wassermann and Sachs-Georgi reactions agree in about 98% of cases in the hands of different observers. In parallel examinations of 214 serums there was complete accord between the Wassermann and Sachs-Georgi reactions in 203 cases, or about 95%; the Meinicke modification agreed with the Wassermann in 208 cases, or over 97%. Of the 11 cases of discrepancy between the Wassermann and Sachs-Georgi reactions, the latter was positive in 5 cases of cured syphilis when the Wassermann was negative, indicating a greater sensitivity of the new test. Of the 6 other cases—all undoubtedly non-

syphilitic—the Wassermann was positive in 3 when the Sachs-Georgi was negative, and in the remaining 3 cases the reactions were reversed. This shows that even with the new test there is no absolute specificity. There was a discrepancy between the Wassermann and Meinicke tests in 6 cases: in 4 of these syphilis could in all certainty be excluded, but the Wassermann was positive and the Meinicke negative; in the remaining 2 cases the reactions were reversed. It would thus appear that the specificity of the Meinicke reaction is somewhat greater than that of either the Wassermann or Sachs-Georgi reactions. Of 12 cerebrospinal fluids examined in the same manner the three reactions corresponded in 11; in the remaining case (a syphilitic woman with nephritis) the Wassermann was faintly positive, whereas the Sachs-Georgi and Meinicke were both negative. In 2 cases of malaria the Wassermann was positive, the Sachs-Georgi positive in one and negative in the other, while the Meinicke was negative in both. Both the Sachs-Georgi and the Meinicke modifications have the advantage over the Wassermann reaction of permitting the omission of extraneous hemolytic amboceptor, guinea-pig complement and sheep's red cells, all of which may be sources of error.

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**The Wassermann and Sachs-Georgi Reaction in the Serum Diagnosis of the Tertiary Forms of Syphilis.**

*Corrado Sestini, Riv. crit. di clin. med., 22:361, Florence, Nov. 5, 1921.*

Although the value of the Wassermann reaction is indisputable, the technic is so complicated and costly as to make its universal application impracticable. Numerous attempts have been made to provoke a visible precipitate. Sachs and Georgi, starting from the concept that the Wassermann reaction is at bottom caused solely by diminution of the degree of dispersion of globulins not directly appreciable by the customary technic, have proposed a simple reaction in which these changes are rendered visible in the form of a flocculation. The reaction has two distinct phases, in the first of which the lipoids in the extracts and the colloids in the serum react, thus corresponding to the reaction between antigen and antibody in the process of complement fixation; the second phase comprises the characteristic modification of the globulins which in the Sachs-Georgi is manifested by flocculation, while in the Wassermann reaction it leads to complement fixation. Extract of beef-heart (1 part in 5 of alcohol shaken for twenty-four hours) is concentrated to one-fourth of its original volume. To 100 c.c. of this are added 200 c.c. of alcohol and 13.5 c.c. of 1% cholesterol. This extract is diluted with physiologic saline solution at the moment of use, first taking equal parts of each, then adding 4 volumes of the latter. The mixture thus formed has the property of provoking complete hemolysis with normal serum, heated for one-half hour at 56° C., and of inhibiting hemolysis with serum surely syphilitic. Of this mixture 0.5 c.c. are added to 1 c.c. of the serum to be examined, already heated, and diluted to 1:10. This is placed in the incubator for two hours, and the results read after being kept from eighteen to twenty hours at ordinary temperature. The serums should then be completely clear, and should be examined promptly. A positive reaction is indicated by a visible precipitate consisting of minute flocculi. A negative reaction contains none of these. Between these two extremes there are variations of intensity. The

author made experiments to compare the results of this reaction with that of the Wassermann in 100 cases of tertiary syphilis, classified as well treated, incompletely treated, and not treated, the disease having been contracted from four to twenty-four years previously. In 91 cases the results were identical by both methods. In 9 cases they were different, 7 of these being among those completely treated. The Sachs-Georgi method proved less sensitive in these, and gave a negative reaction in the face of a positive Wassermann. On the other hand, among those not treated, it was positive in a case where the Wassermann was negative. It is wise to make both tests whenever possible.

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**Chemical Composition of the Flocculi Occuring in the Sachs-Georgi Reaction for Diagnosis of Syphilis.**

*M. Klostermann and W. Weisbach, Deutsch. med. Wchnschr., 47:1092, Sept. 15, 1921.*

For this study, quantities of 500 c.c. each of luetic serum, 3 to 4-plus, were mixed with 2,000 c.c. physiologic salt solution and 1,250 c.c. Sachs-Georgi-extract solution. Albumins are altered by high temperature and no longer split into albumin and globulin, some varieties of albumin lose much of their solubility if dried in vacuo. Weight of the moist precipitate was therefore determined directly. Ether-soluble substances (lipoids) were first separated from ether-insoluble ones. The resulting mass weighed 0.2025 gm.; the consistency was that of firm fat; numerous crystals were scattered through it. The filtrate was separated into its component lipoids and fats. By saponification with alcoholic potash, the fats were rendered ether-soluble; the remaining pure lipoids were saponified. The new filtrate of pure lipoids weighed 0.0685 gm.; after crystallization it proved to be almost pure cholesterol. The remaining solution, clarified by extraction with ether, contained the saponified fats. After conversion into fatty acids with HCl, the product was extracted with ether and washed with small quantities of distilled water to remove all HCl. After evaporation of ether the mass weighed 0.0312 gm. From the ether-soluble portion of the precipitate were thus isolated 0.0312 gm. fatty acids and 0.0685 gm. pure lipoids, totalling 0.0997 gm.; the original precipitate gave 0.2025 gm. ether-soluble substances. About one-half consisted of fatty acids and lipoids. The portion containing ether-soluble (albuminous) substances was now separated into portions, respectively soluble and insoluble in salt solution. Only a small part went into solution; this might consist of globulin and albumin, but was probably albumin, on account of the slight solubility. The solution was carefully neutralized, then mixed with equal parts saturated solution of ammonium sulphate. The salted-out mass weighed 0.004 gm., consisting of globulin. Albumin remained in the filtrate. Qualitative tests with heat and acetic acid, the biuret reaction, nitric acid, ninhydrin, were all negative; after long standing, there was slight clouding with potassium ferrocyanid and acetic acid. Since the last test is not specific and others were negative, the solution was albumin-free. Treatment of the flocculi with 0.85% NaCl solution dissolved out only globulin, albumin being found absent. There now remained only the portion insoluble in physiologic salt solution. This was placed on a weighed filter. On account of unavoidable contamination with cotton, a Kjeldahl nitrogen determination was made, showing 0.0218 gm. albumin;

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half the quantity was therefore albumin, the rest impurities. Since albumin not previously altered may go over and is relatively readily soluble in salt solution, and since the precipitated globulin becomes more insoluble, the insoluble remaining portion was therefore globulin. During the investigation it remained for almost 8 days precipitated and only a very small quantity was soluble in salt solution. An approximate summary of the results may be made, as follows: Lipoid is to albumin as 9:1. Globulin in water occupies about 7 times its dry volume, the relation being 9:7, and the globulin mass acting as a powerful colloid. The Sachs-Georgi extract studied contained 0.244 gm. ether-soluble substances per 200 c.c., most of them being demonstrable in the coagulated flocculi. The study strongly supports P. Schmidt's interpretation, that before precipitation the globulins act as precipitants, the colloid of the extract as a precipitated colloid. The globulins surround and discharge the electrically negative charged extract particles.

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**Hecht and Sachs-Georgi Modifications of the Wassermann Reaction.**

*Alessandro Radaeli, Gior. Ital. d. mal. ven., 62:506, Milan, Oct. 28, 1921.*

Of the various modifications of the classical Wassermann reaction, only Hecht's and more recently Sachs-Georgi's have obtained wide use. Hecht's original modification was proposed to simplify Wassermann's complicated technic and to avoid possible changes in the serum by heating; it omitted inactivation and used the natural complement and hemolysin, eliminating from the reaction the guinea-pig serum and hemolytic amboceptor. This reaction was subsequently further modified by titration of the complement and hemolytic amboceptor of the serum to be tested. The Hecht reaction has many adherents who claim to obtain better results than with the Wassermann reaction, especially in early or mild infections, congenital syphilis, old or insufficiently treated cases, and syphilis of the central nervous system. The so-called dissociated reaction (negative Wassermann with positive Hecht) is taken to indicate a mild infection which is either on the way to recovery or to an aggravation of symptoms. One advantage claimed for the Hecht reaction is that it is frequently positive in cases with a negative history, without clinical signs of syphilis, and with a negative Wassermann. In Salouraud's laboratories the Hecht modification is used in all cases along with the original Wassermann, and a sort of official recognition was accorded it in France following its adoption by a commission appointed to study the problem of marriage among syphilitics.

Later Sachs and others showed that physical changes in the serum caused various changes in its biologic reactions, e.g., inactivation of the complement by the mere dilution with distilled water. Sachs maintained that this change was due to a modification of the serum-globulins, more particularly their manner of suspension or solution in the serum. As to the mechanism of this change in immunity reactions he asserted that there was first produced an antigen-antibody compound which acted upon the globulins causing a disturbance in their suspension; secondly, the globulins thus disturbed were precipitated and carried with them those component portions which take part in the complement reaction. Thus Ehrlich's theory was amplified to the extent of explaining that the first

cause of the inactivation of complement was always the formation of this antigen-antibody compound; but, instead of acting directly on the complement, this compound acted on the globulins, altering their physical state and thus bringing about an inactivation of the complement. In its application to the Wassermann reaction this explanation was somewhat far fetched, since no actual antigen is employed but extracts of normal organs. The difficulty was overcome by assuming that the lipoids in the organ extracts acted on the globulins exactly like antigens. Why this should happen only with the globulins of a syphilitic serum has so far not been explained. The conception of Sachs, therefore, is that the Wassermann reaction is due to a physical change in the state of the globulins in a syphilitic serum, and he has attempted to demonstrate this physical change in the suspension of the globulins by a visible serum flocculation, just as in the Wassermann reaction there is a visible hemolysis or absence of hemolysis. Sachs and Georgi have subsequently shown that the addition of definite quantities of cholesterol to the alcoholic organ extracts intensifies the reaction, which is a visible flocculence of greater or lesser density when cholesterolized alcoholic extract is added to a syphilitic serum.

The author has applied both the Hecht and the Sachs-Georgi tests, as well as the Wassermann reaction, to the serums of 204 dispensary patients, syphilitic and nonsyphilitic. In 90% the three tests coincided. In a few cases of latent but undoubted syphilis, with a negative Wassermann, the Hecht modification was positive; the Sachs-Georgi reaction proved less sensitive than the Wassermann. Both the Hecht and the Sachs-Georgi tests were apt to be positive in subjects manifestly free from syphilis. The Hecht modification is recommended as a dependable confirmation of the Wassermann reaction; the Sachs-Georgi reaction may be used either as a control of the Wassermann or in its stead, as an aid in diagnosis.

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#### Bruck's Seroreaction in Tropical Africa.

*R. Mouchet, R. van Nitsen and P. Walravens, Compt. rend. Soc. de biol., 85:720, Paris, Oct. 22, 1921.*

Physicians of the French colonies frequently encounter syphilis and framboesia, but usually have no means of employing the Wassermann reaction. In seeking a suitable substitute, the authors were impelled to study Bruck's reaction. In this method, 0.5 c.c. of the patient's unheated serum is placed in an ordinary reaction tube; 2 c.c. of distilled water and 0.3 c.c. of 25% nitric acid (sp. gr. 1.149) are added. The mixture is shaken and set aside for ten minutes. A heavy precipitate is produced. Then 16 c.c. of distilled water are added and the tube is slowly inverted three times. With a negative reaction the precipitate redissolves, the result being read after twenty-four hours. A sediment if 0.5-1 cm. deep, indicates a 1+ reaction; if 1-2 cm. deep, a 2+ reaction; if more than 2 cm. deep, a 3+ reaction. Tests were made on 32 caucasians and 56 negroes. In syphilis and framboesia, Bruck's reaction is positive when the Wassermann is positive. Malaria gives a negative Wassermann and usually a positive Bruck. Practically every (African) native has malaria. Nearly all the negroes tested gave a positive Bruck. Syphilitic

or frambesic natives treated with arsenobenzol had a negative Wassermann, the Bruck remaining positive. Bruck's reaction cannot be substituted for the Wassermann test.

(1e—82)

**Study of the "Four Reactions" in Syphilis.**

*C. Goedhart, Nederl. Tijdschr. v. Geneesk., 65:2190, Haarlem, Oct. 29, 1921.*

The author has examined the blood and lumbar fluid of 88 syphilitic patients who had already been tested by the so-called 4 reactions of Nonne. Eighteen patients had shown more or less serious symptoms of the central nervous system: the other 70 were cases of syphilis of long standing and of latent syphilis. Puncture was made some time after the end of treatment, when the Wassermann reaction was negative and no special symptom indicated an affection of the nervous system. Among these 70 cases, 51 patients showed entirely normal spinal fluid. In 19 cases changes were found. The Nonne reaction was positive 17 times; in 14 cases there was opalescence, 3 times pronounced turbidity. There was slight lymphocytosis 7 times, in 2. In two of these cases there was lymphocytosis only.

The Wassermann reaction was positive (2-plus to 4-plus) 5 times, but never positive alone. Leaving out of consideration the 10 cases where the Nonne reaction alone was feebly positive and the 2 with lymphocytosis alone, there remain 7 cases in which several reactions are positive. In all these cases, the blood Wassermann reaction was negative and there were no particular complaints or symptoms showing affection of the central nervous system. In certain cases there was a possibility of meningitis. In the early periods of treatment particular attention was paid to the Wassermann reaction. However, even in case of a negative Wassermann reaction there may be relapses and this reaction does not give any indication as to the spinal fluid. The author reports several cases in which, despite a negative Wassermann reaction, the spinal fluid reactions were positive, and for which, therefore, he had given further treatment, in most cases with good results. He consequently advises intermittent mixed antisyphilitic treatment to be begun as early as possible, controlled by examinations of blood and spinal fluid, and if a meningitis appears, with or without symptoms, to repeat the treatment until the reactions become negative, whereupon a further blood and spinal fluid test is necessary.

(1e—83)

**Colloidal Reactions of the Cerebrospinal Fluid.**

*A. Sordelli and F. Renella, Rev. Asoc. méd. argentina, 35:137, Buenos Aires, Aug., 1921.*

The Wassermann reaction is not 100% specific in syphilis. Many more sensitive tests have been devised, but these are less specific than the Wassermann. It remains to try out all the reactions, the less specific and more sensitive, and also the more specific and less sensitive, until there is discovered the ideal test which will be both specific and sensitive in the highest degree. The authors tested out the various reactions of Nonne, Wassermann, Lange, Emmanuel, and of Guillain, Lachelle and Larroche, the three latter being designated as colloidal tests. Lange's colloidal gold test is more difficult technically, but the results were found

to correspond closely with those of the Wassermann test, as did also those of the benzoin colloidal test. The use of colloidal tests is urged to corroborate the Wassermann, though a scrupulous technic must be employed. A positive reaction with the colloidal test must be accepted by itself, for though these tests are the most delicate they are the least specific.

(1e-84)

**The Gold Sol Reaction.**

*J. K. Mayr, Archiv. f. Dermat. u. Syph., 134:243, Leipzig, July 20, 1921.*

This paper reviews the theories and practical application of the gold sol reaction. One hundred serums were tested with the gold sol but the reaction was not applicable to blood serum. In using some solutions of the gold sol, almost 100% agreement between it and the Wassermann reaction was found, but with the same serums and other gold solutions, no such results were obtained. The statement is made that the gold solutions are not yet sufficiently uniform, and that the fault lay with them. The suggestion is made that the gold sol solutions be prepared at a central laboratory and distributed from there as needed to ensure uniformity. When set up for blood serum, 24 tubes are used, which brings the last tube to a dilution of 1:40,000,000. A good bibliography is appended.

(1e-85)

**Comparative Value of the Colloidal Benzoin Reaction.**

*H. Rabeau, Compt. rend Soc. de biol., 85:704, Paris, Oct. 22, 1921.*

Two hundred tests were made of the sensitivity and specificity of the reaction, checked by comparison with the Bordet-Wassermann. The original method was used. Of the cerebrospinal fluids examined 112 were from clearly syphilitic cases, and 88 from individuals with no evidences of syphilis. The reaction nearly always agreed with the Bordet-Wassermann. The test is simple and responds only to syphilis. It is rarely doubtfully negative where the Bordet-Wassermann is feebly positive, but is always negative if syphilis is absent. It is superior to the colloidal gold test, which has a delicate technic and limited significance, and superior to the Sachs-Georgi test. It should rank with the Bordet-Wassermann test which it confirms and interprets.

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**Colloidal Reactions of Benzoin and Mastic in Cerebrospinal Fluid.**

*Salvador Mazza, Carlos Mey and Flario Niño, Rev. Asoc. méd. argentina, 35:134, Buenos Aires, Aug., 1921.*

Simultaneous tests were made on 110 specimens of spinal fluid with the Wassermann reaction, the mastic colloidal reaction, and the benzoin colloidal reaction. It was found that both colloidal reactions coincided more or less closely with the Wassermann test. The Wassermann test was effected with 1 c.c. of fluid; the benzoin reaction was done with 5 tubes and 1 control and employment of a saline solution of 0.1 per thousand; the mastic test was carried out with 4 tubes and 1 control, with an electrolytic solution of 1.25% stabilized with 0.50 of 1% potassium carbonate. The colloidal reactions are not more sensitive than the Wasser-

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mann for the diagnosis of syphilis of the central nervous system. The reactions do not differentiate between general paralysis, tabes or early cerebrospinal syphilis, but they do serve to distinguish between secondary syphilis with meningeal involvement and early syphilis of the neuraxes.

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**Technic of the Colloidal Benzoin Reaction.**

*G. Guillain, G. Laroche and P. Lechelle, Compt. rend. Soc. de biol., 85:776, Paris, Oct. 29, 1921.*

The authors consider the technic of Sordelli and Rennella, presented during August, 1921, at the biological meeting at Buenos Aires, inadequate, in that the granules of benzoin are partially dissolved by alcohol; one of the conditions essential for colloidal suspension is therefore violated. The reaction is thus made less sensitive and curves resulting therefrom are abnormal.

(1e—88)

**A Note on the Preservation of Cells in Spinal Fluid as Measured by the Cell Count.**

*C. J. Campbell, L. M. Davidoff and G. P. Grabfield, Boston M. & S. J., 185:657, Dec. 1, 1921.*

The authors refute the teaching that cells in spinal fluid disintegrate so rapidly that the count, in order to be accurate, must be made as soon as possible after withdrawal. A large proportion of their laboratory work is on spinal fluids, and it is often inconvenient to count the cells promptly. If the cells disintegrate as rapidly as had been supposed the sending of fluids any great distance for examination would be precluded. It was therefore attempted to determine the keeping qualities of the cells in spinal fluids under various conditions. The tabulated results show that the count of cells immediately on withdrawal was identical with recount about six hours later. The cell count of fluids placed in the ice-box remained unchanged for seven or eight days. At room temperature during hot weather the cells remained intact for five or six days. Incubated fluids never lasted more than three days. At the end of 24-48 hours many bacteria were noted, the fluids not having been handled with aseptic precautions. The study makes apparent that if nonpurulent fluids be preserved at room temperature or in the ice-box and well shaken before counting, the cell count will be correct for at least five days after withdrawal.

(1e—89)

**Effect on the Wassermann Reaction in the Spinal Fluid when Inactivated by Different Degrees of Heat.**

*H. Eicke, Med. Klin., 17:1273, Berlin, Oct. 20, 1921.*

At the dermatologic branch of the Rudolf Virchow Hospital in Berlin, comparative tests in cases of paralysis have shown that Wassermann reaction with the spinal fluid is least affected by inactivation. The fluid in each case was tested with and without inactivation as it was possible that the different results would justify conclusions as to prognosis and differential diagnosis. By using different temperatures for inactivation it was established that in cases of paralysis an inhibiting body which  
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is very resistant to heat is formed in the fluid. This body seems to be related in a certain way to the euglobulin fraction which is precipitated at 33% saturation. As the inhibiting body which is found in all other syphilitic diseases of the central nervous system, is much less thermostable, it is possible that a differential diagnosis might be made by using different temperatures for inactivation. Five cases of paresis with negative blood and positive spinal fluid reactions, had positive Wassermanns with the fluid when they were inactivated in the ordinary way at 56° C. These cases which were considered paresis, showed unusual reactions in the spinal fluid. Further investigations are necessary in order to establish whether the clinical pictures of these cases also show deviations from the classical course.

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**Notes on the Formalin Blood-Test for Syphilis.**

*C. Suffern, Lancet, 2:1107, London, Nov. 26, 1921.*

The value of the test lies in its simplicity. Blood is drawn in the usual manner as for a Wassermann test, and collected in a clean but unsterilized test-tube, stopped with cotton-wool. It is placed in a rack for twenty-four hours, at room temperature, at the end of which time the serum is decanted into another clean but unsterilized test-tube. A drop of ordinary commercial formalin is added and the tube is plugged with cotton-wool. The serum and formalin are allowed to remain at ordinary room temperature as before for twenty-four hours, at the end of which time an observation is made. Coagulated serum is a positive result, fluid serum a negative result. Out of 11 cases the Wassermann and formalin reactions agreed in 8. Of the remaining 3, it is highly probable that 2 formalin tests were confused, and that the formalin results really agreed with the Wassermann reactions, making the total 10 out of 11.

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**Action of Formol on Normal and Pathologic Serums.**

*Papacostas and Gâté, Compt. rend. Soc. de biol., 85:869, Paris, Nov. 12, 1921.*

The authors found in 1920 that the addition of 3 drops of commercial 40% formol to the serum of syphilitic patients with a positive Wassermann reaction gelatinized the serum in from twenty-four to forty-eight hours, but that this reaction did not occur in nonsyphilitic serum. They considered this gelatinization with formol a specific reaction, always positive with a positive Wassermann. They have now discovered a reaction to formol in both syphilitic and normal serums. Serum is put in a series of tubes, 1 c.c. in each. Minute, gradually increasing, quantities of formol are added. With a certain amount of formol, small granules appear in the clear fluid; with a slightly larger amount, the fluid becomes green and opalescent; a larger quantity produces opaque milky clouds which fall to the bottom of the tube. Still more formol produces coagulums which float in the clear liquid like milk curds. This ends the reaction, and more formol does not cause further change. This gradual precipitation of albumin from serum by minute but gradually increasing quantities of formol, occurs in normal and pathologic serums, whether syphilitic or not. But if the tubes in the last stage of the reaction are set aside for a day, the fluid above the curds

gelatinizes if the serum is syphilitic. This does not always occur, however, but seems to depend on the thoroughness with which the albumin has been precipitated. Precipitation of serum albumin by formol is, therefore, not a specific reaction, but gelatinization of the serum by 3 drops of formol in thirty-six hours is a syphilitic reaction paralleling the Wassermann reaction.

(1e—92)

**Positive Wassermann Reaction in Typhus Fever.**

*Karl Bauer, Münch. med. Wchnschr., 68:1251, Sept. 30, 1921.*

The statements of the author are a result of serologic investigations which he had made as a prisoner of war at Nikolsk. In the records of the tests, he has collected the results of tests of 50 serums of patients with no history of syphilitic infection. It was shown that the Wassermann reaction with inactivated serum is almost always positive in typhus fever when the blood specimens are taken before the crisis. The serum, up to a few days before the crisis, shows a strongly positive reaction. Shortly before the fever stops, the reaction decreases progressively until it becomes negative a few weeks after the crisis. In doubtful cases when the Weil-Felix reaction cannot be made and there is a question as to the diagnosis between typhus and typhoid fever, the author decides in favor of typhus when there is a positive Wassermann, particularly as he always found a negative Wassermann in many cases of typhoid and paratyphoid.

(1e—93)

**Effect of Heating Horse Serums in the Bordet-Gengou Diagnostic Reaction for Dourine.**

*A. Bessmans, Compt. rend. Soc. de biol., 85:889, Paris, Nov. 12, 1921.*

Diagnosis by complement-deviation has shown certain variations; thinking such variation due possibly to differences in heating, the author made a series of heat tests, which are illustrated by curves. Conclusions: 1. Normal horse serum contains variable quantities of substances capable of producing non-specific complement-deviation with the dourine antigen. These substances are much reduced by heating for thirty minutes at 56° to 58° C. They practically disappear on heating for half an hour at 60° C. 2. For sero-diagnosis of dourine by the Bordet-Gengou reactions, serums must be inactivated by heating for a minimum of thirty minutes at 60° C. Falsely positive reactions are avoided in this way. 3. With the same technic, it is theoretically possible that certain slightly positive serums may escape detection. Practically, such serums occur only in recent infections or intensive treatment, as in syphilis in man.

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**Ray's "Hemolytic" Test in Kala-Azar.**

*Richard H. P. Sia, China M. J., 35:397, Shanghai, Sept., 1921.*

Ray found that if a small quantity of the patient's blood (2 drops) was added to 10 times its volume of distilled water, the mixture quickly cleared and became transparent, in malaria, but that in kala-azar it remained turbid and, on standing, formed a white flocculent precipitate. Tests in other diseases associated with splenomegaly were negative. The

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only conditions other than kala-azar in which Sia obtained positive tests were certain severe forms of anemia of uncertain etiology. The writer has employed this test in the case of 86 patients suffering from various diseases, and of 10 normal individuals. He found that positive tests were obtained only in the case of kala-azar patients, and that in all the cases of kala-azar there was a positive reaction.

(1e-95)

**Comparative Studies in the Chemistry of Blood and Cerebrospinal Fluid.**

*Grete Egerer-Seham and C. E. Nixon, Arch. Int. Med., 28:561, Nov. 15, 1921.*

Quantitative studies were made, as far as possible in the same individuals, of the acid-base equilibrium, of sugar, urea, and creatinin content, and enzymatic activity of blood and cerebrospinal fluid, in various diseases, with normals for controls (97 subjects in all). Methods are stated and results tabulated. Conclusions in regard to sugar content of cerebrospinal fluid, taking 0.069% as the normal value, with 0.095 as maximum and 0.045 as minimum normal, show: The quantity of sugar is approximately normal in cerebrospinal syphilis, tabes dorsalis, syphilis, hemoplegia, disseminated sclerosis; neurasthenia, brain tumor, arteriosclerosis. In diabetes, sugar in spinal fluid increases proportionately to blood-sugar. Sugar tends to slightly increase in dementia paralytica and hysteria, but not sufficiently for diagnosis. There is decrease in sugar in tuberculous and epidemic meningitis. The ratio between sugar content of spinal fluid and blood in normal individuals is 56.2, with a maximum of 70.3 and a minimum of 47.8. No increase of sugar in spinal fluid constant with its increase in the blood is apparent in normal subjects. Similarly no constant increase is found in pathologic cases. Creatinin value in normal spinal fluid varies from 0.45 to 2.20 mg. per 100 c.c. Ratio between creatinin of normal spinal fluid and blood shows still greater variability than for sugar, and in pathologic fluids the ratio for creatinin is not sufficiently constant for clinical application. For urea, the average value in 100 c.c. of normal spinal fluid is 9.87 mg., with extremes at 7.53 and 12.75. Urea content of cerebrospinal fluid in cerebrosyphilis is about the same as the normal maximum. The average ratio of urea in normal spinal fluid and blood is 62.15%; this is slightly raised in cerebrospinal diseases. Determinations of acid-base equilibrium in cerebrospinal fluid in pathologic and nonpathologic subjects show that, under normal conditions, the carbon dioxid carrying capacity of the cerebrospinal fluid is somewhat lower than that of blood, while in acidosis it is greater in some instances. Lipase was suggested in only 2 fluids among 26 in various diseases. Diastase was present in 28 of 30 fluids; highest in spastic torticollis; low in 2 cases of meningitis. Specific gravity, in all determinations, averaged 1.0086. Taking 1.058 as the specific gravity of blood in normal adults (Hammersten), the ratio between the specific gravities of the two fluids is 95.35. In syphilis, the cerebrospinal fluid showed no constant deviation from normal in sugar, creatinin, urea, acid-base equilibrium, specific gravity or enzymatic activity.

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**The Action of Carbon Dioxid on Salt and Water Distribution in the Blood.**

*Genko Mukai, J. Physiol., 55:356, London, Nov. 18, 1921.*

Experiments were performed with defibrinated dog's blood, the blood being drawn from a cannula in the carotid artery of a dog under chloroform and ether anesthesia. Special care was taken to use the blood as soon as possible. The first experiments were designed to determine the distribution of salts and water in the blood at various tensions of carbon dioxid. The defibrinated blood was divided into two portions, Sample A, which was exposed to the air, and Sample B, which was equilibrated with CO<sub>2</sub> in a large flask that contained almost pure CO<sub>2</sub>. Four factors were determined: (a) The volume percentage of the corpuscles; (b) the solids; (c) the ash as sulphate, and (d) chlorin content. The tabulated results show that under the influence of carbon dioxid (1) the corpuscles increase in size by taking up water from serum; (2) the percentages of the solids and ash of serum increase; (3) the total amount of ash as sulphate remains the same in serum as a whole when allowance is made for the loss of water, which shows that cations do not pass from corpuscles into serum and that there is no interchange of base between them, and (4) the total amount and concentration of chlorin of the serum decrease, and this must have entered the corpuscles. As previous workers have shown, these changes are reversible and parallel in response to the variations of CO<sub>2</sub> tension. To determine the CO<sub>2</sub> carrying capacity of serum, defibrinated dog's blood was divided into two portions, Sample A (blood), and Sample B (serum). The latter was obtained by centrifuging. Both samples were divided again into six portions, each of which was equilibrated, respectively, with the air and with air containing 75, 112, 153, 186 and 223 mm. CO<sub>2</sub> at room temperature. All portions of Sample A were then centrifuged under liquid paraffin and the serum was separated. CO<sub>2</sub> in the serum was determined by Van Slyke's method. Tabulated results show the influence of corpuscles on the CO<sub>2</sub> capacity of serum. Both Samples A and B change their CO<sub>2</sub> content in accordance with variations of tension, but the former is more liable to such change than the latter. This different behavior of serum is attributed to the varying distribution of salts and water in blood under CO<sub>2</sub> treatment. As long as serum is in contact with corpuscles and these alterations are reversible, serum contains a definite quantity of CO<sub>2</sub> at a given tension, no matter whether the tension is decreased or raised to that degree. After separation, serum is free from the influence of the corpuscles and carries CO<sub>2</sub> by its own capacity. It was also determined experimentally that CO<sub>2</sub> in blood is approximately equally distributed between corpuscles and serum at every tension of carbon dioxid. When blood is treated with CO<sub>2</sub>, both corpuscles and plasma increase in osmotic pressure. If CO<sub>2</sub> is led through a sample of plasma which has been separated from corpuscles, the increase of osmotic pressure is decidedly less than in that in which it has not been separated. The difference of osmotic pressure is due to the alteration of the CO<sub>2</sub> carrying capacity of serum. To determine whether the osmotic pressures are equal on both sides of the corpuscles, Hamburger's experiment (freezing point determination) was repeated and it was found that the corpuscles had a lower osmotic pressure than

the plasma both in normal blood and in blood treated with CO<sub>2</sub>. By Barger's microscopic method the author determined the molar concentration without losing CO<sub>2</sub> and proved that the law of osmosis is perfectly applicable in the case of blood treated with CO<sub>2</sub>.

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**Blood Studies in the New-Born. Morphologic; Chemical; Coagulation; Urobilin and Bilirubin.**

*William Palmer Lucas, Bradford French Dearing, Hal R. Hoobler, Anita Cox, Martha F. Jones and Francis Scott Smyth, Am. J. Dis. Child., 22:525, Dec., 1921.*

Williamson has determined the amount of hemoglobin in grams per 100 c.c. of blood. He found that on the first day it was about 23.25 gm. and gradually went down till it reached 12.57 gm. during the second year of life. The authors estimated the hemoglobin of young infants and found that from the first to the twelfth days of life the daily average percentage was 117, 114, 110, 114, 107, 113, 109, 103, 103, 97, 98, and 91, respectively. It has been stated that the hemoglobin percentage of jaundiced babies is lower than the normal, but this was not confirmed in these studies. The red cell count is highest during the first week of life and then gradually decreases, corresponding very closely to the hemoglobin estimation. Nucleated cells were found in 52% of all infants studied on the first day of life and in 5% on the second day. There was quite a variation in size in the early days, both larger and smaller cells being numerous. Hemolysis occurred very easily so that "ghosts" were fairly frequent. A leukocytosis was observed in the new-born, which during the first week was definitely due to the polynuclear cells; after this the polynuclears gradually declined to the same level as the lymphocytes. The lowest platelet count was on the eighth day, when it reached 196,000. Chemically there was a definite drop in the nonprotein nitrogen, urea and creatinin and a definite rise in sugar and carbon dioxid. The calcium content of the plasma is higher in the newly born infant than in older children. The plasma content was constant throughout the studies. During the first 4 days of life there was prolongation of the coagulation time which it is believed bears some relation to the so-called hemorrhagic diseases of the new-born. It was not possible to demonstrate urobilin in the stools of infants up to 10 weeks of age. Bilirubin was detected in the plasma during the first week of life in many cases and seemed to correspond to the icterus.

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**The Measurement of the Oxygen Content of the Mixed Venous Blood, and of the Volume of Blood Circulating per Minute.**

*J. Barcroft, F. J. W. Roughton and R. Shoji, J. Physiol., 55:371, London, Nov. 18, 1921.*

It was sought to devise a simple method to measure the oxygen content in the venous blood with sufficient accuracy for many purposes. By breathing nitrogen in the manner described later it is believed an equilibrium may be produced between the mixed venous blood and the alveolar air in the lung. The partial pressure of oxygen in the alveolar air is then a measure of the partial pressure of oxygen in the mixed

venous blood of the lung capillaries at the moment. This blood differs from the normal mixed venous blood inasmuch as it is depleted to some extent of CO<sub>2</sub>. On this account the oxygen pressure is too low. By the application of an empirical correction an approximation to the proper oxygen pressure can be obtained, being as close to the correct value as other collateral errors in any case would admit. The method of respiration was as follows: a bag, fitted with a tap and valves, as described by Douglas, was filled with nitrogen. The valves and tap were so disposed that the subject of the experiment could inspire at will either from the external air or the bag, but expiration was in neither case into the outer atmosphere. The experimental subject then followed this procedure: (1) He clipped his nose; (2) breathed through the valves, inspiring atmospheric air till he was breathing normally; (3) made a rather deep expiration; (4) turned the tap so that the next inspiration came from the bag; (5) inspired rather deeply from the bag and then breathed normally for several respirations; (6) turned the tap on the bag so as to shut it; (7) with his mouth closed and taking no further inspiration he turned to a Haldane gas analysis apparatus fitted with an alveolar air tube and obtained a sample of his alveolar air. This process should take about six seconds. The person who is conducting the experiment notes the interval between procedures 4 and 6 with a stop-watch. This is known as the "interval of nitrogen respiration," and does not include the time taken over Procedure 7. The actual time occupied in the establishment of the equilibrium is therefore about six seconds longer than the "interval of nitrogen respiration."

The results are plotted graphically and by means of detailed mathematical formulas it is believed the coefficient of utilization of oxygen from the blood may be measured within almost 10%, from which the minute-volume may be calculated to a corresponding degree of accuracy.

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**The Direct Measurement of the Partial Pressure of Oxygen in Human Blood.**

*J. Barcroft and M. Nagahashi, J. Physiol., 55:339, London, Nov. 18, 1921.*

The authors describe in considerable detail their method for the direct measurement of the partial pressure of oxygen in the human blood. The apparatus, illustrated in the article, consists of a specially devised gas analyzer and saturator. The procedure consists of withdrawing from an artery or vein by direct puncture about 10 c.c. of blood to which is exposed a small bubble of alveolar air at 37° C. until an equilibrium is established between the blood and the bubble. The blood is then analyzed. It was possible to measure the oxygen pressure in blood drawn directly from a blood-vessel in man to within about 2 mm. The observation of previous workers on the great range of unsaturation of blood from the basilar vein when the arm is exposed to widely differing temperatures is confirmed.

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**The Determination of the Gases of the Blood.**

*Donald D. Van Slyke and William C. Stadie, J. Biol. Chem., 49:1, Nov., 1921.*

In this paper the authors first describe and illustrate a modification (Sec. 1—Page 180)

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of the original macro form of gas apparatus described by Van Slyke in 1917. The modification consists chiefly of a reduction in bore of the upper graduated stem of the apparatus from 4 mm. to 2.7 mm. thus increasing the length of the tube holding 1 c.c. of gas from 75 or 80 mm. to 150 or 160 mm. The tube is divided into 100 instead of 50 divisions. In this finer tube gas volumes can be estimated to 0.1 of a division, or 0.001 c.c. In extracting the gases the apparatus is so manipulated that the blood mixture is whirled about the wall of the chamber. Inversion of the apparatus is not recommended. It is necessary to use the apparatus in a room in which the temperature does not vary by more than 1° C., or to provide the apparatus with a water jacket. When an accurate measurement of very small gas volumes (less than 0.05 c.c.) is desired, as may be the case in determining the N<sub>2</sub> or CO content of blood, it is desirable for measurement to increase the gas volume by reducing the pressure. The reduction is accomplished by holding the levelling bulb lower than it would be placed in order to put the gas in the apparatus under atmospheric pressure. For this purpose the authors have found 500 mm. of mercury to be a convenient reduction in pressure.

The authors performed a number of determinations of the nitrogen gas content of blood, both as drawn from the veins and after equilibration with air at room temperature. They found that the same results were obtained when no reagents were added as when ferricyanid was used to release the oxygen, or acid to release carbon dioxid. In the series reported in this paper the nitrogen was determined by extraction in a vacuum without the addition of reagents. The apparatus employed was the model with the finer bore measuring tube described above. The tabulated results show that the blood, both in the veins and after aerating at room temperature, contains about 0.5 volume per cent. more nitrogen gas than calculated from the solubility of the gas in water. The authors include as "nitrogen" all the gas extracted by evacuating blood and left after absorption of oxygen and carbon dioxid.

For the determination of oxygen, they recommend certain changes in technic. They have reduced the amount of potassium ferricyanid per c.c. of blood from 60 or 70 mg. (0.4 c.c. of saturated solution for 2 c.c. of blood) to 10 mg. The ferricyanid solution used contains 20 gm. per 100 c.c. Of this 0.1 c.c., containing 20 mg. of the salt, is used for 2 c.c. of blood. The smaller amount of ferricyanid causes as rapid and complete an evolution of oxygen as do larger amounts and it has 2 advantages over the latter: First, the smaller amount does not appreciably retard laking and it is therefore unnecessary to wait for laking to become complete in the apparatus before the ferricyanid is introduced; furthermore, the possibility of error from incomplete laking is eliminated. Second, reduction in the amount of ferricyanid reduces the somewhat annoying amount of precipitate formed by interaction with the mercury in the apparatus. The authors also recommend the use of water instead of ammonia for laking blood. In Van Slyke's original procedure (1918) the blood, before addition of ferricyanid, was laked in the apparatus with saponin in a dilute ammonia solution the proportions of blood and ammonia being those previously adopted by Haldane and by Barcroft in their methods for the determination of blood oxygen. The authors found that the use of such a mixture may introduce 2 errors: (1) the alkalinity of the mixture is not sufficient to prevent the escape of carbon dioxid entirely in all cases; (2) the alkaline reaction accelerates

some oxidative process by which part of the oxygen freed is slowly consumed. Hence when the oxygen is freed in too alkaline a solution, the entire amount is not obtained. At present the authors use water for laking the blood, which seems to obviate the error due to oxygen consumption. The 10 to 20 volumes per cent. of carbon dioxid that accompany the oxygen, are removed after the extraction by absorption with NaOH solution, before the O<sub>2</sub>+N<sub>2</sub> volume is measured. Consequently, the danger of error from admixture of CO<sub>2</sub> with the O<sub>2</sub>+N<sub>2</sub> is also avoided. The elimination of ammonia has an additional advantage in reducing the insoluble black precipitate which forms in its presence by the interaction of ferricyanid and mercury. With water as diluent and a reduction in the amount of ferricyanid employed, the precipitate is practically nil.

The authors have also made some modification in the method of determining the carbon dioxid in whole blood and plasma. The 1% ammonia solution used for washing out the cup of the apparatus before each determination has been dispensed with and at present the cup is merely rinsed with water before each determination and then into it is run 1 c.c. of distilled water. The blood or plasma is run under this layer of water. For decomposing the blood bicarbonate, lactic acid instead of sulphuric acid is used, the lactic acid being made up with sufficient accuracy for the purpose by diluting 1 volume of concentrated acid (specific gravity 1.20) to 10 volumes with water. For absorption of the carbon dioxid in the mixture of gases obtained after extraction of whole blood, the authors find half normal NaOH preferable to the 10% KOH recommended by Van Slyke in 1917.

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**A Mechanical Shaker and Other Devices for Use with the Van Slyke Blood Gas Apparatus.**

*William C. Stadie, J. Biol. Chem., 49:43, Nov., 1921.*

The gas apparatus is clamped to a metal upright but at a sufficient distance from it to permit a to and fro motion, accomplished by connecting the neck of one of the bulbs to a pulley by means of a piston-like bar. Rotation of the pulley by an electric motor at the desired speed produces a back and forth motion of the apparatus.

The author remarks that for accurate pressure adjustment it is desirable to use an empirically calibrated scale which may be attached at some convenient place on or near the stand holding the apparatus. The scale is calibrated by placing in the chamber of the gas apparatus an amount of water equal to the final volume of the reaction mixture to be used (e. g., 8 c.c. for oxygen analysis of 2 c.c. of blood). Then, with the upper cock of the apparatus open, to establish atmospheric pressure within, one marks on the scale the levels at which the surface of the mercury in the levelling bulb is held when 0.10, 0.20, or 0.30 c.c. of gas are present in the apparatus. In subsequent analyses the levelling bulb is adjusted by comparison with the scale thus prepared. When a separatory funnel is used as a tonometer for saturation of blood with gas, the funnel may be conveniently rotated by an apparatus illustrated in the article. The stem of the funnel is slipped into a rubber tube which fits over the axle of a pulley turned by a motor. To secure even distribution of the blood about the inner wall, the separatory funnel is so arranged

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that its lower side is horizontal. The proper position may be attained either by suspending the neck of the funnel in a wire loop or by laying the funnel in a horizontal trough.

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#### The Action of Acids on Blood and on Hematogenic Tissues.

*Heinrich Brieger and Fritz Breitharth, Ztschr. f. d. ges. exper. Med., 25:111, Berlin, Oct. 14, 1921.*

It has frequently been stated that poisoning with acids, notably inorganic acids, is followed by a leukocytosis. The rapid conversion of organic acids into carbon dioxide probably explains their milder effect. Forschbach and Brieger observed marked leukocytosis after poisoning with a 40% ointment of potassium chromate. Severe lesions and tissue necrosis occurred in various organs. This in itself was capable of causing leukocytosis, due to irritation of the bone-marrow, but the likelihood of cutaneous absorption of the chromate as chromic acid led to the supposition that the leukocytosis was due, in part, to the poisoning by the acid.

The authors have studied the effects of chromic acid on the blood-picture in guinea-pigs. Chromic acid (or potassium chromate) was injected intravenously during anesthesia. By taking blood-counts for comparison, before and after injection, while the animal was under the influence of the anesthetic, the leukocytotic effect of anesthesia was ruled out. Intravenous injections of normal salt solution, as such, had no effect on the blood-picture. The increase in the number of leukocytes, under the influence of chromic acid, is proportional to the amount of poison injected. Potassium chromate will cause leukocytosis, but not until the salt contains 100 times the amount of chromium, is its action as marked as that of chromic acid. Thus the elementary chromium cannot be the factor concerned in causing leukocytosis. If, in the first injection, the animal receives a large amount of chromic acid, a slight initial leukopenia (8,200) is followed by a rapid increase (34,500). If one begins with smaller doses, the initial leukopenia does not occur, and the increase is more gradual. Before the kidneys show serious lesions, myeloid changes are found in the bone-marrow, which explain the leukocytosis.

The fact that the intensity of the reaction is not dependent upon the chromium content makes it probable that the effect produced is due to free hydrogen-ions; this view is supported by the blood-picture, which reveals serious cell lesions, anisocytosis of the erythrocytes, vacuolization of the leukocytes—more especially the lymphocytes—degeneration of the polynuclear cells; an altered resistance of the erythrocytes, and the reduced production of metahemoglobin and oxyhemoglobin. Chromic acid is a weak acid, but the still weaker arsenous acid produces the same effect.

Thus far, the investigations have not been sufficient to determine the exact influence of the diminished alkalinity of the blood in these reactions. When potassium chromate is introduced through the skin, in a salve, it may be assumed that it reaches the organism as chromic acid. However, the action of the chromate introduced intravenously, qualitatively the same, although quantitatively much weaker, cannot be traced to the acid. Probably the explanation is the same as for the parallelism

between the action of phosphoric acid and of the phosphates—namely, in acid solutions the sexivalent chromium has a much greater oxidizing power; one must also reckon with the appearance of trivalent chromium.

It may be mentioned that, in the author's experiments, a very slight deflection of the neutrophil cells to the left could be noted. Contrary to this, in human cases of poisoning by chromic acid through ointments, Brieger found up to 21% myelocytes. This is due to extensive tissue necrosis, and in some cases to uremia.

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**Calcium Content in the Blood of Various Species.**

*P. Mazzocco, Rev. Asoc. médica argentina, 35:141, Buenos Aires, Aug., 1921.*

The calcium content in the cells and in the plasma or serum of blood is the same in the same species, whether in citrated or hirudinized blood. Calcium exists, although in small quantities, in the nucleated as well as the non-nucleated red corpuscles. The quantity of calcium in the serum or plasma of the same species is about equal, and the calcium of the corpuscles affects the total amount of the blood calcium.

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**The Calcium Content of Blood-Plasma and Corpuscles in the New-Born.**

*Martha R. Jones, J. Biol. Chem., 49:187, Nov., 1921.*

A series of observations on the calcium content of the blood of normal infants ranging in age from four hours to twelve days. Approximately 15 c.c. of blood were taken by means of a syringe from the superior longitudinal sinus about four hours after feeding. Lyman's nephelometric method was used, the technic described by Jones and Nye being employed. On 22 infants 68 determinations were made. The average values were found to be as follows: Whole blood, 8.8 mg. per 100 c.c.; corpuscles, 5.0 mg. and plasma, 12.3 mg. The average for plasma was found to be higher than that reported in older children while corpuscle and whole blood values were less. The twelve days included in the series of observations were divided into six periods of two days each and the results of the analyses made during each period averaged and plotted. The plasma values remained constant throughout, while there was a tendency for the corpuscle averages to decrease and those of whole blood to increase. The author found that during the twelve day period the average percentage of red blood cells dropped from 55 to 41.9.

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**A Simple Method of Quantitative Estimation of Calcium in the Blood.**

*Richard Weiss, Deutsch. med. Wchnschr., 47:1298, Berlin, Oct. 27, 1921.*

Weiss describes a special filtration apparatus designed for estimating the calcium percentage in blood by the Von de Waard method. By this method instead of the normal of about 12 mg. calcium per 100 c.c. of blood, it is found that in tetanus, there is only 4 mg. of calcium in 100 c.c. of blood. On the other hand, in certain other diseases there

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is an increase of the calcium content up to as much as 18 mg. per 100 c.c. The estimation of the calcium content of blood has, in the author's opinion, considerable value in diagnosis, for example, in typhus fever, for determining the cause of the hemorrhages.

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**Quantity of Calcium in the Blood.**

*R. Kummer and G. Minkoff, Compt. rend. Soc de biol., 85:863, Paris, Nov. 12, 1921.*

The authors have tested the method of Kramer and Tisdall in 20 subjects. The quantity of calcium ranged from 0.080, to 0.130 parts per 1000. Jansen's figure is 0.090, Stehmann's 0.086 to 0.092. The maximum error for the method is stated as 5%; the authors' error was 3 to 10%, the larger variation being ascribed to unfamiliarity with the technic.

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**Reduction in the Blood during Pregnancy. Labor and the Puerperium.**

*J. Olow, Compt. rend. Soc. de biol., 85:827, Paris, Nov. 5, 1921.*

Studies made by Bang's micromethod gave the following results: (1) During the latter part of pregnancy, the reduction is about the same as in non-pregnant women. However, the daily variations are more distinct, without regard to food, especially in toxemias. Here the maximum is double that of non-pregnant women, and more than a third higher than during normal pregnancy. (2) During labor, the reduction does not exceed normal limits, in certain cases; usually, however, it is increased, the maximum generally occurring at the end of labor. In 2 or 3 cases, it occurred an hour or two after. (3) During the puerperium, there is striking lability and much variation, daily, or at different hours of the same day. Sometimes there are marked single elevations, much exceeding the normal; in general, such elevations correspond to those noted during labor, which are sometimes exceeded. The time of the elevation varies in different cases; equal daily variations have been observed from three to seven days after confinement, on the second day, and from eight to ten days postpartum. (4) The reduction in the blood of the umbilical vein is nearly always from 0.01 to 0.04% less than in the maternal blood.

(1e—108)

**Studies of the Sugar in the Blood of Pigeons.**

*Hannah Elizabeth Honeywell, Am. J. Physiol., 58:152, Nov. 1, 1921.*

The blood-sugar of normal pigeons was first determined. The blood was drawn directly from the heart into a 0.2 c.c. pipette by means of a long hypodermic needle, and the amount of sugar estimated by MacLean's micro-method. The tabulated results show, for one bird, a variation from 150 to 200 mg. glucose per 100 c.c. blood, and for the other bird 140-215 mg. glucose per 100 c.c. blood. These figures represent the highest and the lowest figures obtained on different dates during the experimental period (about three months). The variations are well within the limits of error for the method and may therefore be considered constant. They show also that there is a con-

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centration of sugar which is characteristic of the blood of a given bird. The birds were then subjected to such sudden changes in external environment as rough handling, loud talking, noise, etc., and a subsequent increase in the blood-sugar was found. But it was found that an inanition period of forty-eight hours has practically no effect on the blood-sugar of the pigeon. When 1 gm. of glucose or less is fed to pigeons there is very little modification of the sugar in the blood, but when 2 or 3 gm. are fed there is a manifest rise in the blood-sugar, which gradually approaches its former level.

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**A Simple, Quick and Exact Two-Drop Method for the Quantitative Determination of Blood Sugar.**

*Richard Weiss, Münch. med. Wchnschr., 68:1255, Sept. 30, 1921.*

The blood sugar content measured when fasting, and then again after ingestion of a certain amount of carbohydrates, gives a much better view of disordered assimilation, than the determination of the sugar in the urine. The reduction method is best for this examination. Fehling's and Bang's method however, when used with very minute quantities of blood, do not show the end results distinctly. By adding ammonia to the alcoholic solution No. 2, however, even in extreme dilutions, a solution so deep blue is obtained that it serves as an excellent indicator. By a method of titration indicated by the author and for which he has constructed a small apparatus, it is possible also to determine the sugar content of the blood in a very simple manner, as follows: With a capillary pipette, 0.1 c.c. blood is dropped into a small test-tube, containing a little absolute alcohol, the alcohol being drawn into the pipette several times in order to bring every trace of blood into the test-tube. The blood mixture is allowed to stand one-half hour, with frequent shakings and is filtered through a small hard filter, while alcohol is steadily poured into the glass of the apparatus. Afterward the alcohol is evaporated, and 0.3 c.c. each of Pavy I and Pavy II, as well as 1.8 c.c. distilled water is added. A cork with a burette is put into the tube which is placed over a moderate fire on asbestos netting, and brought to a slow boil. As soon as the fluid commences to boil, the glass tube is removed and burette with a stop-cock substituted for it in which the one-hundredth normal glucose had been sucked up to highest mark and the cock is opened so that the blood sugar solution can drip in. After every drop the cock is closed and the reaction awaited. After the decoloration has been completed, the blood sugar reaction is read. The 2 Pavy solutions, 0.3 c.c. of each, require 0.0003 gm. blood sugar to decolorize. Consequently, what has been consumed in the 1/100 N solution after deduction of 0.0003 (i. e., the glucose consumed by the titration plus the sugar contained in the blood serum) is altogether 0.0003. As the quantity added by titration is known, the difference shows the sugar content of the blood. In order to obtain a complete adjustment of the blood sugar solution, it is necessary by a preliminary test by the same method to determine the titer of the glucose solution.

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**Lipemia.**

*W. R. Bloor, J. Biol. Chem., 49:201, Nov., 1921.*

The purpose of this paper is to present additional data on the blood lipoids in persistent lipemia, especially that of diabetes and of hem-  
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orrhage. It presents in tabulated form the results of detailed study of 5 cases of diabetic lipemia in human subjects and, similarly, a detailed study of the blood lipoids in hemorrhagic lipemia in 4 rabbits and a dog. In a preliminary discussion of persistent lipemia, the author states that the lipemia produced by a single fat feeding disappears normally within twenty-four hours; persistence after this time is probably to be regarded as pathological. This does not apply in cases of continuous or forced fat feeding. The greatest number of cases of persistent lipemia are found in diabetes. According to Bloor the characteristics of persistent lipemia, as shown by available evidence are: (1) In lipemia of whatever origin, all 3 blood lipoids (fat, lecithin, and cholesterol) are increased, the fat generally showing the greatest ultimate increase and cholesterol next. (2) There is perceptible, in most cases, a sequence in the appearance and disappearance of these lipoids, fat being the first to increase, lecithin next and cholesterol last; during the disappearance of the lipemia, the fat diminishes first and the cholesterol last. High values for lecithin and cholesterol often persist for some time after the fat has reached approximately normal values. (3) In most instances the values for the ratio of lecithin to cholesterol are markedly below normal, due to the greater increase of cholesterol. (4) The fat which produces the lipemia may be of endogenous or exogenous origin or both; the phenomena of the lipemia are the same in either case. (5) The cause of the lipemia being regarded as a disturbance of the balance between inflow and outflow of fat in the blood, the immediate causative factor in the hemorrhagic lipemia is probably an abnormally large inflow of fat while in diabetic lipemia it is an abnormally slow outflow.

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**Observations on Blood-Fat in Diabetes.**

*N. R. Blatherwick, J. Biol. Chem., 49:193, Nov., 1921.*

The author determined in diabetic patients the total blood-fat (fatty acids plus cholesterol) by the method of Bloor (1917). The methods of Folin and Wu and of Shaffer and Hartmann were used for blood sugar determinations. All blood samples were taken in the postabsorptive condition before breakfast. The results are given in a series of charts in the article which show the percentage values for blood fat and blood sugar and the diet in grams of carbohydrate, protein and fat for the day preceding the blood sample. The author believes his study of blood fat in relation to the fat in the diet shows that cases of mild and moderate diabetes are apparently able to utilize satisfactorily large amounts of fat, as indicated by the constancy of the blood fat level and by the absence of acetone bodies in the urine.

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**The Cholesterin Content of the Blood-Serum of the New-Born.**

*Roberto de Simone, Pediatria, 29:1023, Naples, Nov. 15, 1921.*

All authors agree today that cholesterin has a defensive function in the organism, due to its antihemolytic and antitoxic action by which it controls the formation of antibodies. Its origin seems to be twofold: synthetic, or endogenous, i.e., by the action of the suprarenal capsules (in the female also of the corpus luteum), and alimentary or exogenous. Few studies have been made of infants. The author undertook a series

of observations on 27 children of ages ranging from 2 to 17 days, using Grigaut's method of measurement, which does not require more than 2 c.c. of serum and gives results of sufficient exactitude. He found that the amount of cholesterin increased gradually with the age and was in direct proportion to the weight of the body, children of considerable weight but of little age having an amount of cholesterin almost equal to that of older infants of lesser weight. The more robust children, having better defensive powers, showed a higher percentage. The diminution of amount in children with hereditary lues was striking. In most cases in which the Wassermann reaction was positive such a diminution occurred, showing the diminished defenses of the organism which has a syphilitic taint. In the case of 2 children prematurely born, with negative Wassermann reactions, the percentage of cholesterin was large in proportion to the size and weight, but this may have been due to the fact that they were twins, and therefore had a relatively light weight. In another child of premature birth, who was syphilitic, the amount of cholesterin was greatly diminished.

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**Cholesterinemia in Man in Various Morbid Conditions.**

*Carlo Alessandri, Riforma med., 37:1095, Naples, Nov. 19, 1921.*

Experiments were made to establish the relation between the suprarenal capsules and cholesterinemia. After the exclusion as far as possible of influences which might cause variation (such as alimentation, a state of fatigue or rest), 1 c.c. of adrenalin solution 1:1,000 was injected both intravenously and subcutaneously. To measure the cholesterin in the blood-serum Grigaut's colorimeter was used. A table of 22 cases shows the diseases, and the amounts of cholesterin. The results show wide variations, even in the same disease. Two tables show the effects on cholesterin content and on blood pressure in 10 cases of different diseases, one-half hour after injection of adrenalin, 5 being intravenous and 5 subcutaneous. The result in the latter was more marked. Comparison of the result of cholesterin content with variation of arterial pressure, showed that after intravenous injection, at the moment in which there was diminution of pressure, there was always increase of cholesterin. After subcutaneous injection there was variation in results, taking these one-half hour later; in 2 cases (diabetes, articular rheumatism) the arterial pressure was slightly increased while the cholesterin reached the lowest values; in the 3 others the pressure was diminished while the cholesterin was the most increased. Increase of cholesterin was not stronger where there was already an excess of it. In 2 cases of chronic articular rheumatism and in one of exudative pleurisy the amount of cholesterin was nearly normal both before and after injection; but in another of chronic articular rheumatism, there was an increase of 0.68 gm. per thousand, greater than in any other case; in 2 of glycosuria there was a slight increase; but in 2 diseases of the nervous system (neurasthenia and sciatica) there was either equality or diminution. It was therefore demonstrated that the results in values of cholesterinemia are different in different diseases. The experiments show that the use of adrenalin causes the mobilizing not only of the cholesterin of the cortical part of the suprarenals but also (and perhaps even in greater quantity) of that deposited in the various tissues of the organism.

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**Simplified Method for Determining Nonprotein Nitrogen in the Blood.**

*A. Grigaut and J. Thiéry, Compt. rend. Soc. de biol., 85:812, Paris, Nov. 5, 1921.*

This method follows the process of destroying organic matter by trichloracetic acid and copper in a sulphuric acid medium. It eliminates centrifugation. A reagent is employed to avoid cloudiness. (1) Nessler's reagent: KI, 12 gm.; HgI<sub>2</sub>, 15 gm. NaOH, 180 c.c.; distilled water, enough to make 1,000 c.c. The cloudy liquid produced is allowed to stand, the perfectly clear liquid being decanted as needed. Perfect clearness is essential. The reagent must stand three months before use. It should not be stoppered with rubber, on account of formation of mercuric sulphid. (2) Sulphuric acid, 100 c.c. with 0.5% solution CuSO<sub>4</sub>, 100 c.c.; (3) 0.2% solution trichloracetic acid. (4) Standard solution (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub>: Dissolve 4,716 gm. of the pure, dry salt in one liter of N/5 H<sub>2</sub>SO<sub>4</sub>, to prevent mould. Remove 10 c.c. and dilute to 1 liter. Each cubic centimeter corresponds to 0.01 mg. nitrogen. Technic: Remove blood albumin by equal volume 20% trichloracetic acid. Shake and filter. In a very large pyrex test-tube are placed 2 c.c. of the filtrate, 1 c.c. of the CuSO<sub>4</sub> solution and a glass bead. The tube is placed on a support, strongly heated to remove water, then more gently heated as charring begins. Continue heating to complete decolorization, until only a faint blue tint (copper) remains. Cool and wash into a graduated flask, add distilled water enough to make 80 c.c. In a second graduated flask, place 25 c.c. standard ammonium sulphate solution, 1 c.c. of the copper sulphate solution and water to 80 c.c. Volume in both flasks is made up to 100 c.c. by adding the Nessler reagent. Mix. If the tint of the two solutions is the same it indicates 0.25 gm. non-protein nitrogen per liter, the normal blood content. Difference in tint may be measured with Duboscq's colorimeter. In azotemia, or for the corpuscles, a smaller quantity of blood should be taken, in order to secure a color-shade approximating the standard.

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**The Use of Sodium Sulphate as the Globulin Precipitant in the Determination of Proteins in Blood.**

*Paul E. Howe, J. Biol. Chem., 49:93, Nov., 1921.*

The method of Cullen and Van Slyke for the determination of fibrin, globulin, and albumin nitrogen of blood plasma, has one objection, and that is the use of ammonium sulphate as the globulin precipitant. This is objectionable for two reasons: (a) because of the use of an ammonium salt which must be removed before determining the globulin nitrogen and (b) because of the physical difficulties involved in the removal of this nitrogen with magnesium oxide. The chief objection to the use of sodium sulphate is the necessity of working at temperatures above 34° C. for precipitation at the highest concentrations of the salt. The solubility of Na<sub>2</sub>SO<sub>4</sub> + 10 H<sub>2</sub>O increases gradually up to approximately 10° C., and then rapidly to 34° C.; above 34° C. the anhydrous salt is in equilibrium with water and the solubility of the salt decreases gradually. Working at incubator temperatures, conditions in regard to solubility are those which hold true in general with magnesium sulphate and ammonium sulphate; i. e., a gradual

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change in solubility with each increment of temperature. In determining the optimum concentration of sodium sulphate for the precipitation of the total globulins, the author contrary to the findings of previous workers, found a critical zone and indications of more than one critical zone by using concentrations of sodium sulphate which differed from the preceding member of the series by 1% of the anhydrous salt. Critical zones in the curve representing the precipitation of protein with increasing salt concentration have been located at 13.5 to 14.5, 17.4, and 21 to 22% of anhydrous sodium sulphate at 37° C. For the purpose of estimating the quantity of protein present at these zones, 13.5, 17.4, and 21.5% of sodium sulphate is recommended.

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**An Effect of the Ingestion of Colostrum upon the Composition of the Blood of New-Born Calves.**

*Paul E. Howe, J. Biol. Chem., 49:115, Nov., 1921.*

It was found that the blood serum of a new-born calf before it has nursed does not contain euglobulin nor pseudoglobulin I. After the calf has received colostrum the blood serum contains relatively large amounts of these substances. On the other hand, if the calf is given ordinary whole milk from a cow well along in lactation, or receives milk from a cow which has not been "dried off" before parturition, i. e., has been milked up to or close to the time of parturition, conditions in which very little globulin is ingested, the quantity of euglobulin or pseudoglobulin in the blood is negligible. The subsequent ingestion of colostrum after a period of twenty-one hours as observed thus far, results in the appearance of the globulins in the blood. These facts relate to blood serum.

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**The Determination of Proteins in Blood. A Micro Method.**

*Paul E. Howe, J. Biol. Chem., 49:109, Nov., 1921.*

The determinations described in this paper can be performed with the usual laboratory apparatus and require but 0.5 c.c. of plasma or serum for each determination. The procedures involve the precipitation of fibrinogen with calcium chlorid, the globulins with definite concentrations of sodium sulphate at 37° C., and non-protein nitrogen with trichloracetic acid. In the case of fibrinogen and non-protein nitrogen the technic of Cullen and Van Slyke is followed. The globulins are precipitated by adding a concentration of sodium sulphate which is greater than the required percentage by the amount of sodium sulphate necessary to produce the desired percentage when added to the blood sample. The solutions are prepared by dissolving the required quantity of sodium sulphate in a little less than the final volume, which requires heat for the higher percentages, and then diluting to volume at 37° C. All precipitations and filtrations with sodium sulphate are carried out in the incubator or hot room. The following concentrations of sodium sulphate are needed: 14, 18 and 22.2%. When 15 c.c. portions of these solutions are added to 0.5 c.c. of blood the final concentrations are approximately 13.5, 17.4, and 21.5% of sodium sulphate respectively. At 13.5% of sodium sulphate, euglobulin is precipitated; at 17.4%, euglobulin and pseudoglobulin I are precipitated and at 21.5% all globulins are thrown out of solution. In case blood plasma is used

fibrinogen is present in each case and the nitrogen representing this protein must be deducted. Suitable blanks must be made for each determination. Precipitations are made in test-tubes or 50 c.c. centrifuge tubes and then closed with a rubber stopper. The filtrations are conducted in the incubator using a dry 9 cm. filter paper. For measuring, the accurately calibrated Ostwald pipettes and the 15 c.c. graduated pipettes introduced by Folin are used. The nitrogen determinations are conducted in large Pyrex test-tubes in general according to the original micro procedure of Folin and Farmer and the distillations are carried out according to the procedure of Folin and Wu, without cooling the distillate. For titrations the author uses standard hydrochloric acid and sodium hydroxide which are approximately 0.05 and 0.025 N respectively. Methyl red is used as an indicator. The author's determinations are as follows: Plasma is collected so that it contains 0.5% of potassium oxalate. Both plasma and serum are centrifuged until clear.

Total Nitrogen: 0.5 c.c. of plasma or serum is placed in a large Pyrex test-tube and the 2 c.c. of concentrated sulphuric acid, 1 drop of 5% copper sulphate, and a quartz pebble are added; the solution is digested over a free flame until clear; heat seven to ten minutes longer. Cool for three to five minutes, then add 25 to 30 c.c. of ammonia-free distilled water, a small amount of talcum powder or powdered pumice stone and concentrated sodium hydroxide solution sufficient to neutralize the acid; then distil into standard acid. For the determination of fibrinogen, 0.5 c.c. of plasma is measured into a tube; 14 c.c. of 0.8% sodium chloride solution at room temperature are added, then 1 c.c. of 2.5% calcium chlorid and a small crystal of thymol and the tube is stoppered. The tube and contents are allowed to stand until the fibrin is formed and then filtered on a dry filter. Two 5 c.c. portions of the filtrate are taken for analysis. For the determination of euglobulin 0.5 c.c. of plasma or serum is measured into a tube, 15 c.c. of 14% anhydrous sodium sulphate at 37° C., and a little thymol are added; the tube is stoppered, shaken and allowed to stand for at least three hours, or until the precipitate has settled. The solution is then filtered through a dry filter and two 5 c.c. portions are taken for analysis. The results represent euglobulin in the case of serum and fibrinogen plus euglobulin in the case of plasma.

Euglobulin Plus Pseudoglobulin I. The procedure is the same as for euglobulin except that 18% sodium sulphate is used. Total Globulins. The procedure is the same as in euglobulin except that 22% of sodium sulphate is used. Non-Protein Nitrogen. 0.5 c.c. of plasma or serum are measured into a tube and 15 c.c. of 5% trichloracetic acid at room temperature are added. The remainder of the procedure is the same as in euglobulin.

(1e-118)

**The Identity of Hemoglobin in Human Beings.**

*G. S. Adair, J. Barcroft and A. V. Bock, J. Physiol., 55:332, London, Nov. 18, 1921.*

(1e-118)

This paper gives an account of investigations to determine whether there are any considerable differences in the hemoglobin of different persons. Preparations were made by slow dialysis of blood against distilled water. These preparations simulated solutions in appearance

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but since they contained intact, though swollen corpuscles they gave dissociation curves widely varying from those of true aqueous solutions of hemoglobin. Solutions of hemoglobin were then prepared, all the corpuscular elements being absent, and the identity of the curves which these solutions yielded was tested. From the blood of the same subjects samples of hemoglobin were made as follows: After defibrinating and centrifuging with 8% NaCl the 50 c.c. of blood from each subject, the cake of corpuscles in each tube was laked by the addition of ether, about 50% by volume of the corpuscles. The mixture was well shaken and the tubes placed on ice for an hour. After centrifuging the preparations showed three distinct layers: (1) ether at the top, (2) a pale pink layer of stroma, and (3) at the bottom a deep-red, clear hemoglobin solution. After partly removing layers (1) and (2) a fine pipette was pushed down and the hemoglobin solution was aspirated. The hemoglobin solutions were placed in two collodion membranes and clipped. After two and one-half days' dialysis, the conductivity of the two solutions was equivalent to a 0.00485 solution of NaCl, taking N/10 as the standard for comparison. The oxygen dissociation curves yielded by these solutions were indistinguishable.

(1e—119)

**Conditions Causing an Unequal Distribution of Erythrocytes in the Blood-Stream.**

*Ernest F. Bostrom, Am. J. Physiol., 58:195, Nov. 1, 1921.*

In these experiments (made on cats) the methods, frequently mentioned in the literature as producing an increase in the number of red cells per unit volume, were used, viz., adrenalin injected directly into the circulation, asphyxia produced by the administration of illuminating gas, and abdominal pressure caused by manual manipulation, by placing weights on the abdomen, or by pumping oxygen or air into the peritoneal cavity until the intraperitoneal pressure reaches about 10 mm. of mercury. Samples for counting were taken practically simultaneously from the capillary blood and from the blood in the left ventricle. The tabulated results show that the increase of red cells is not uniform throughout the circulation. More cells are found in the capillary blood than in the heart blood after the application of abdominal pressure, and after the administration of adrenalin or illuminating gas. It was observed in the experiments with adrenalin that the greatest increase in number of red cells was found when the temperature of the skin was strikingly lowered through the peripheral vasoconstriction. The accumulation of red cells in the peripheral tissues is associated with one or both of the following factors: (a) a lowering of the surface temperature; (b) a decrease in the oxygen supply to the tissues. To test this assumption counts of blood samples were made, taken from the heart and from the skin capillaries just above the knee, before and after a ten minute immersion of the cat's foot in ice water. It was found that a cold application could cause a rise in the capillary blood-count even beyond the area where the temperature is actually lowered. A local increase in the H-ion concentration, brought about by a subcutaneous injection of a dilute acid solution (acid sodium phosphate), was followed by an increase in the number of erythrocytes per cubic centimeter in that part. There are good reasons for assuming an increase in the H-ion concentration in the peripheral tissues after the adminis-

tration of adrenalin, asphyxia and abdominal pressure. Such an increase in the H-ion concentration explains the peripheral accumulation of red cells, as it causes the red cells to lose, partly at least, their negative surface charges, which tend to prevent the cells from adhering to one another and to the walls of the vessels.

(1e—120)

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**Studies on the Fragility of the Red Blood-Cells.**

*Roy M. Greenthal and William S. O'Donnell, Am. J. Physiol., 58:271, Dec. 1, 1921.*

The authors ascertained the effect of certain substances on red cell fragility in saline solutions. In most instances the substances were added to the blood *in vitro* but in other experiments the red corpuscles were allowed to remain in contact with the substance for a time and were then washed free and tested for fragility. The fragility of the red blood-cells was increased after treating them with carbon dioxide gas, and hypertonic (5%) saline solution; the fragility was decreased by treatment with 6% sodium bicarbonate solution and also by Fowler's solution. The fragility of the red corpuscles was tested in 3 patients with cardiac disease and cyanosis; in each case an increased fragility resulted. No marked change in fragility was found in 4 surgical cases that had been subjected to ether anesthesia, nor did CO gas, adrenalin, atropin, diphtheria or tetanus antitoxin have any effect on the fragility of red corpuscles.

(1e—121)

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**Experimental Anemia Produced by Saponin.**

*J. Firket, Compt. rend. Soc. de biol., 85:727, Paris, Oct. 22, 1921.*

The reported study was suggested by the autopsy of a case of grave anemia of 4 months' duration. The postmortem findings were atypical. Symptoms did not correspond to those of pernicious anemia, pure aplastic anemia, or intoxication. In addition to the diagnostic problem, the findings suggested another, viz., whether a poison that maintains the bone-marrow in its usual fatty condition also prevents myeloid formation in liver and spleen. It has been shown that saponin is a powerful hemolytic agent producing aplastic anemia with myeloid metaplasia of the spleen. By experiments with saponin on 45 rabbits, it was determined that the resistance of washed red corpuscles to the poison does not vary. The resistance of washed red corpuscles of splenectomized rabbits is the same as that of the red corpuscles of normal rabbits, but cells of splenectomized rabbits are more resistant to hypotonic solutions than cells of normal rabbits. Examination of the bone-marrow, spleen, liver and glands disclosed that saponin, far from producing aplasia of the marrow, provokes, in proportion to erythrocyte destruction, an intense reaction of all myeloid tissues with hyperplasia. Notwithstanding absence of bone-marrow aplasia, vascular rupture of congested capillaries in the marrow occurs, the circulation is interrupted, infarcts are produced and are soon replaced by fibrous tissue. Continued treatment with saponin produces almost entire transformation into cicatricial tissue, with hemorrhagic areas in which myeloid elements reproduce without differentiation. Hematopoietic activity continues uninterrupted only in the spleen and liver.

(1e—122)

**A Simple Method for the Determination of the Coagulation Time of Blood in Animals.**

*O. Inchley, J. Pharmacol. & Exper. Ther., 18:237, Nov., 1921.*

The method is a modification of Buckmaster's, and consists essentially in taking up a drop of blood in a fine wire loop and observing when, on slowly rotating the loop by hand, the blood no longer moves freely under gravity. The mean of the time when the first sign of altered mobility appears, and when complete fixation of the drop occurs, is taken as the clotting time. The preparation is maintained at blood temperature in a small moist-chamber, composed of 2 glass cells, used for microscopic purposes, which can be ringed with plasticene and pressed together so as to form a small air-chamber. The preparation is inserted in the air-chamber and held by a clamp, which also serves for rotating. The observation is made under water at 37°—40° C., in sufficient quantity to maintain an approximately even temperature during the experiment; it is convenient to employ a submerged lamp and a reflecting mirror inclined at 45°. Figures, obtained during 2 experiments on rabbits anesthetized with urethane, before and after treatment with calcium introduced by the ionizing current, are given.

(1e—123)

**Rapidity of Sedimentation in Human Blood with Other Considerations on the Blood of Syphilitics.**

*W. Schönfeld, Arch. f. Dermat. u. Syph., 136:69, Leipzig, Sept. 12, 1921.*

Earlier writers have observed this phenomenon in pure undiluted blood. In recent times it has been studied after the addition of substances which retard coagulation, chiefly sodium-citrate solution. Poppert and Wagner have examined the blood from syphilitics and have described the technic of the foregoing experiments. Schönfeld reaches the following conclusions: (1) The corpuscles in a woman's blood separate more rapidly than those of a man's blood. (2) For physiological reasons the latter half of a woman's pregnancy is distinguished by the high degree of sedimentation. (3) A difference in the rapidity of the sedimentation in the blood of syphilitics as compared with that of other morbid conditions is apparent, but was found to be subject to some reservations. (4) The rates of sedimentation of the same patient's blood taken on different days, especially in the first two hours after the withdrawal of the specimen, display great variation; but they become almost identical eight or ten hours later. There is little variation in the sedimentation rate of different specimens taken at the same time. (5) The reason for this sedimentation and its variations in single or multiple specimens has not yet been explained. In all probability it depends on several factors acting in concert, such as some particular property of the blood corpuscles or the influence of external factors.

(1e—124)

**The Clinical Significance of the Rapid Precipitation of Red Blood Corpuscles.**

*J. Schürer and K. Eimer, Berl. klin. Wchnschr., 58:1251, Oct. 17, 1921.*

Red blood-corpuscles sink as soon as solutions like sodium citrate  
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or hirudin which delay coagulation are added to the blood. The time necessary for precipitation may be anywhere from twelve minutes to twenty-four hours. Hastened precipitation may also be observed in sections of ligated vessels. It was noted that red blood-cells sink more rapidly in women, especially in pregnancy. The same holds true in paralysis, tabes and cerebral syphilis.

The authors timed precipitation in 400 cases. When precipitation occurs very rapidly the erythrocytes agglutinate in rolls and clumps, auto-agglutination. In normal blood agglutination is prevented by the negative electric charge of the erythrocytes. The red cells of healthy men wander toward the anode more quickly than those of pregnant women. The increased agglutination and accelerated precipitation in pregnancy is therefore due to a diminished electric charge. Experiments of interchange with plasma and erythrocytes in two tests of rapid and slow precipitation proved that the plasma contains the causative elements. The amount of fibrinogen is not a factor, but the products produced by the splitting of albumin and the interrelation of cholesterol and lecithin may be important. The author found accelerated sedimentation in acute and chronic diseases. The shortest period of sedimentation was noted in acute articular rheumatism. Rise of temperature is not decisive. Rapid precipitation was noted in afebrile diseases, such as arteriosclerosis, gout, Graves' disease, malignant tumors and cirrhosis of the liver, and sedimentation is apparently accelerated in all organic diseases. Purely local diseases (compensated valvular lesions, gastrophtosis, benign pyloric stenosis) are exceptions.

The diagnostic value of the method is small because the reaction occurs too frequently. A probable but not a certain differentiation can be made between pregnancy and myoma of the uterus, articular rheumatism and static symptoms, incipient tuberculous of the apices and nervous fatigue. For pulmonary tuberculosis the sedimentation time was 537 minutes in healthy men, 184 minutes in afebrile tuberculous patients, and 61 minutes in febrile cases. In women the respective times were 291, 139 and 37 minutes. Greatly accelerated sedimentation is a bad prognostic sign in tuberculosis.

(1e—125)

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**Studies on Erythrocytes, with Special Reference to Reticulum, Polychromatophilia and Mitochondria.**

*J. Albert Key, Arch. Int. Med., 28:511, Nov. 15, 1921.*

Altmann regarded his bioblasts as the ultimate divisions of life. A large percentage of these were mitochondria. Different investigators have credited mitochondria with performing a great variety of functions, such as transmission of hereditary characteristics, formation, directly or indirectly, of collagenic fibrils, plant plastids, myofibrils, epidermis fibrils, neurofibrils, pigments, zymogen granules of pancreas, and secretion of other glandular cells, etc. Other investigators believe they have some function related to general metabolism of the cell or connected with its respiration. It is usually stated that in order to demonstrate the mitochondria, the tissue must be fixed within two hours after death. The author was able to stain mitochondria in thyroid tissue six hours after death, and in nerve cells from spinal ganglia of rats, which were fixed twenty-four hours after killing the animal. The presence of mitochondria in young erythrocytes has not been satisfactorily

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demonstrated. Young erythrocytes differ from the mature in that they have lower specific gravity and tend to agglutinate or adhere to foreign bodies. The basophilic substance, generally referred to as reticulum, is characteristic of young erythrocytes. In the unaltered erythrocyte it is distributed uniformly through the hemoglobin-containing part of the red blood-cell, and when fixed and stained gives pictures of polychromatophilia. The reticulum is formed by the union of this basophilic substance with the supravital stain, and its morphology varies with the stain used. The basophilic substance is not of nuclear origin; it is a protoplasmic constituent but is not of mitochondrial nature. Janus green B, though not a specific stain for mitochondria in young erythrocytes, stains the basophilic substance in the form of an irregular net. It is not so reliable a stain for reticular substance as brilliant cresyl blue or azure I or II. It is of value where the erythrocytes contain nuclear fragments, as in an hour or so these are stained pink and can be differentiated from the green reticular substance present in the same cells. The mature erythrocyte is not a living cell. The hemoglobin is contained in a hydrophilic gel which is surrounded by a definite membrane. Study of the mitochondria of the erythrocytes as an indicator of blood regeneration is not recommended because it has not been adequately shown that they are present after the nucleus leaves the cell. Study of the reticulated cells is recommended as a reliable indicator of the presence of young cells in the circulating blood. The form of the reticulum varies in pathologic and hemorrhagic anemias.

(1e—126)

**Thrombocytes and Leukocytes in the Blood and Internal Organs after Intravenous Introduction of Witte's Peptone.**

*S. Seeliger and H. Gorke, Ztschr. f. d. ges. exper. Med., 24:322, Berlin, Sept. 22, 1921.*

Intravenous injection of peptone causes leukopenia which is later followed by leukocytosis. Opinions differ as to the cause of the leukopenia. Some think it due to lytic disturbances, others to retention of the leukocytes in internal organs. Ruechel and Spitta injected from 0.3 to 0.6 gm. peptone, and noted that the leukocytes disappeared almost entirely which they ascribed to abnormal distribution. The condition of the blood-platelets after peptone injection has been studied less. The authors have directed their attention to the relations of the leukocytes and platelets, and especially to the distribution of the blood in the internal organs after peptone injection, in order to determine whether the effects of peptone are connected with anaphylaxis. Biedl and Kraus having claimed that the two processes are identical. Löwit, Friedberger and Besredka contradict this claim, holding that symptoms of peptone poisoning merely resemble those of anaphylaxis, as do numerous other toxic processes. Mautner found that the anaphylactic symptoms could be suppressed in the dog by extirpating the spleen before, or early during sensitization; splenectomy did not influence the signs of peptone poisoning. The authors' numerous experiments in rabbits showed a fall of blood pressure (of 30-50 mm. Hg), a few minutes after peptone injection, which was decreased by ether narcosis; the temperature sometimes fell as much as 3.6°, but sometimes there was a rise; coagulation was delayed, sometimes for more than an hour; urine and feces were passed. The erythrocyte count was not changed. Five minutes after

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injection, the leukocytes were markedly diminished, falling in fifteen to thirty minutes to one-eighth or one-tenth the original number. An increase began in an hour after injection, not attaining the original number; but within six hours, after the animals had recovered from shock, a leukocytosis began, increasing for two days and reaching 40,000 or 50,000. During leukopenia, the lymphocytes were absolutely decreased but relatively increased, the leukopenia occurring chiefly at the expense of the granulocytes. Eosinophils are increased in anaphylaxis, but this was never found in peptone poisoning. The second injection has the same effect upon the blood as the first, and a true anaphylactic eosinophilia of 8-10% may occur. The platelets varied considerably in normal rabbits from 350,000 to 750,000, but were always diminished after injection. Thrombopenia was marked after twenty-four hours. Complete disappearance of the platelets was not observed, even in 2 fatal cases. A second injection produced the same thrombopenia. By simultaneous, intravenous injection of large quantities of adrenalin, leukopenia and thrombopenia were largely prevented, but similar doses, given intramuscularly or subcutaneously, failed to prevent them. In all the animals, peptone injection produced marked venous congestion of the internal organs, which were enlarged and flaccid. Hyperemia was especially noticeable in the bone-marrow. Vascular flaccidity is undoubtedly due to peripheral vasomotor causes, whether to paralysis of the sympathetic, or to stimulation of the parasympathetic, is not determined. The rapid but feeble heart action is probably connected with the venous stasis, as is also the insufficient aspiration occurring with the superficial, purely thoracic respiration. Histologic examination showed marked accumulation of platelets in the venous capillaries of the organs affected by venous stasis. Platelets were most numerous in the spleen, but numerous also in the liver and bone-marrow; only a few were found in the lymph-glands; in the lungs, there were strikingly fewer platelets after peptone injection than normally. Accumulation of platelets was limited to the venous capillaries. Where the capillaries were not completely filled with platelets, these were situated along the capillary walls, abundantly mixed with leukocytes; the red cells were in the center of the lumen; sometimes this order was reversed. Possibly slowing of the blood stream, in connection with the direct effect of peptone on coagulation, might cause thrombosis, the foreign protein liberating thrombokinase from the platelets and leukocytes. Besides the accumulation of platelets, destruction and increased regeneration were evident. Ingestion of platelets by phagocytes, with changes in structure and staining, could be clearly followed. This was most marked in the spleen, but occurred also in lymph-glands and liver (Kupfer's stellate cells). In splenectomized animals, the lymph-glands and liver took part in the phagocytosis of the platelets. Increased regeneration of platelets from megakaryocytes was perceptible in the bone-marrow ten minutes after injecting peptone. Leukopenia occurs because the leukocytes collect in the distended venous capillaries. This accumulation of leukocytes was especially marked in the pulmonary capillaries, whether from mechanical effect of the reduced blood current, or also from negative chemotaxis, is not decided. It can be stated positively that the leukocytes are injured by the peptone injection, to such extent that large numbers are phagocytized. Phagocytosis of erythrocytes, which occurs normally in the internal organs, is greatly decreased. Phagocytosis of leukocytes is ac-

complished by macrophages in the spleen, liver, lymph-glands, bone-marrow and lungs; also by Kupfer's stellate cells, but especially by megalokarocytes in the bone-marrow.

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**Sudden Variations of the Leukocyte Count Due to Immediate Nerve Action.**

*J. Tinel and D. Santenoise, Compt. rend. Soc. de biol., 85:715, Paris, Oct. 22, 1921.*

Modifications of the leukocyte count have been found in certain nervous and mental affections and in normal cases, owing to nervous action. The oculocardiac reflex, when positive, is instantly followed by a leukopenia and by a tendency to an inverted proportion. The fall is progressive, corresponding nearly to the slowing of the pulse, with quick return to normal on cessation of the ocular pressure. The count remains normal when the reflex is negative. The constancy and rapidity of this reaction suggests a vasomotor cause. Experiments were made with ethyl chlorid, electrical stimulation, hot air and amyl nitrite, and differences between the healthy and the paralyzed side in peripheral nerve lesions were studied. Median neuritis with vasoconstriction shows a diminution of 2,000 polynuclears in the region of the nerve. Reflex oculocardiac leukopenia does not appear in the region of paralyzed nerves. Pain and emotion are also believed to be causative of leukopenia. Possibly the leukopenia results from obstruction to flow from vasomotor constriction. The resemblance between leukocyte counts in these experiments and in hemoclastic shock is suggestive. The results are tabulated.

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**Sudden Variation in the Leukocyte Count Produced by Nerve Action.**

*P. Pagnicz, Compt. rend. Soc. de biol., 85:766, Paris, Oct. 29, 1921.*

The author refers to experiments made in 1908 in the dog and rabbit. Leukopenia was observed after stimulation of the vagus and depressor, and was apparently related to the fall in blood-pressure. It is doubtful whether such leukopenia, including that recently reported by Tinel and Santenoise, should be interpreted as a local vasomotor effect, because variation in the count is noted in arterial as well as in venous blood. It more probably results from temporary arrest of the leukocytes in the viscera or along the vascular walls. The mechanism may be nervous, but not purely vasomotor.

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**Clinical Value of Changes in the Differential Leukocyte Count.**

*Hans Werner Wollenberg, Ztschr. f. klin. Med., 91:236, No. 3-6, Berlin, 1921.*

The author considers Schilling's differential method as the simplest and best way of determining the changes in the leukocyte picture. The counting of 200 cells is sufficient if the blood smear and technic of counting (Mäander method of Schilling) are good. The change in the leukocyte picture in infectious diseases furnishes a valuable criterion of the functional reaction of the bone-marrow to the increased demand.

The blood-picture is normally regulated by the so-called "stimulus tonus" of the bone-marrow by which leukocytes are replaced as they are used up, the type and number of the leukocytes remaining constant. Stronger stimulation of the marrow increases the number of leukocytes without a displacement of the picture so long as this function of the marrow is retained. Variations of from 5,000 to 6,000 leukocytes may occur in one day under certain conditions without displacement of the differential picture. This was observed in a patient with mechanical obstruction of the colon. The displacement of the leukocyte picture is always a sign that the marrow is not equal to the demands made on it. Pneumonia causes a hyperleukocytosis and also a displacement of the neutrophil picture to the left because the bone-marrow is not equal to the demands made on it and there is an output of immature leukocytes. The total leukocyte count is of less use than the differential count in a consideration of the condition. Hyperleukocytosis may persist in pneumonia after the crisis as a result of bronchitis, but the differential count remains normal. In a case of pneumonia in which the leukocyte count suddenly fell to normal just before death, the change in differential count became still greater, a sign of decreased function of the bone-marrow. In diseases accompanied by a leukopenia at the beginning, such as typhoid, influenza, measles, and rubella, there is often a marked relative increase of the rod-nuclear neutrophils. Arneth considers these an increase of the output of immature cells while Schilling shows that they are mature forms whose development has been interrupted by the toxic damage to the bone-marrow. The functional damage of the marrow often outlasts the fever.

A displacement to the left in chronic diseases, as tuberculosis, often indicates an acute exacerbation or complication even before there are other symptoms.

In exceptional cases of convalescence from febrile diseases, promyelocytes or very young forms of cells suddenly appear in the blood. This is explained by assuming a strong stimulus to the myeloid tissue other than that of the bone-marrow. The return to normal may be accompanied by immature cells which escaped destruction in the spleen. According to Klieneberger, an atypical variation in the leukocyte count, a fall of 200 to 300% in place of the normal daily rise, occurs in malaria, and is due to digestion. A reduction of the count may occur in other conditions as after puncture in pleurisy with exudate in which there is first an increase in the neutrophils with a reduction of the lymphocytes, followed for eight days by marked variations and reduction of the count in the afternoons. It probably represents a conflict between infection and defense. The variations in malaria seem to be associated with the generation of the parasites. The displacement of the leukocytes remains constant in disease, while there are often marked variations in the total count in one day, and hence the differential count is a better criterion of the course of the disease. Curves showing the displacement percentage at the same hour for several days are of great diagnostic and prognostic value.

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Reports on Differential Blood-Counts and Their Value in  
Protozoal Infections.

*A. F. Cole, China M. J., 35:450, Shanghai, Sept., 1921.*

This report is based upon blood-counts made on 120 unselected  
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pensioners at the West Kent Clinic, drawing allowances for past infections with malaria (all types) from all theatres of war, and even prior to the war. The report is made in answer to specific questions propounded by the Ministry of Pensions: (1) The evidence obtained regarding a relative increase of large mononuclear cells, and its relation to: (a) malarial infection of any type, relapsing or latent. Out of 120 cases of malaria, recent or remote, the percentage of large mononuclears in 53 cases was 8% or more. In 43 it was 10% or more, and in 23 it was 12% or more. Out of 20 cases in which counts were done at intervals, the patients being presumed to take 10 gr. quinin per diem in single doses before breakfast, in no less than 10 the large mononuclear percentage actually increased; in 2 it remained stationary, and in 8 it decreased. The average differential count from the 120 pensioners was as follows: polymorphonuclears, 61%; large mononuclears, 8%; all other mononuclears, 31%. (b) Chronic infection from other protozoa.—In the cases with a history of dysentery, the average differential leukocyte count was: polymorphonuclears, 60%; large mononuclears, 9%; all other mononuclears, 31%. From this it may be deduced that, in the type of cases of dysentery usually observed at this clinic, usually subacute or quiescent, there is no change in the large mononuclear count. The differential count is exactly the same as in the malarial cases studied. (c) The taking of drugs, e. g., quinin, and its influence on the differential leukocyte count.—The writer has been unable to form any conclusion of scientific value with reference to the influence of drugs on the percentage of large mononuclear cells, for various reasons. (2) The value or otherwise of a relative increase of large mononuclear cells, with particular reference to malarial relapses, or latent malarial infections: The mononuclear count is of no value as indicating malarial relapses or latent malarial infections. A minimum relative percentage of 10 indicates an increase of the large mononuclears.

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**An Introduction to the Study of Hematophagy.**

*H. M. Woodcock, J. Roy. Army M. Corps, 37:321, London, Nov., 1921.*

In this instalment hematophagy is considered a normal occurrence, and the nature and origin of blood-platelets and of Kurloff bodies are discussed. If hematophagy indicates the function, which may be exercised by a cell, of ingesting blood-cells and elements of various kinds; little or no attention has been paid hitherto to the effect or result of this process upon the devouring cell. Red-staining granules have been erroneously regarded as per se the nucleus or nuclear material of some parasite. It is important to recognize that certain products of the alteration of the substance of red blood-corpuscules may stain red by Romanowsky stains. The Giemsa stain, though invaluable for blood work, must be controlled by a known reliable chromatinic stain such as hematoxylin. Without the use of both types of staining, it would have been impossible to study hematophagy. In these experiments human blood, and the blood and hematopoietic organs of the guinea-pig and kitten were used. Blood-platelets are not to be considered complete cells, because they possess nothing of the nature of a nucleus; they do not consist of unaltered nuclear material, because they have no chromatin. Platelets are bodies consisting of protoplasm, with which is associated a

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relatively considerable amount of intensely staining substance which is regarded provisionally as some iron compound. A clue to their origin was suggested by a study of the Kurloff bodies, particularly by their appearance in films. Investigation of the macrophages (large mononuclears, or transitionals, and megalokaryocytes) disclosed that the platelets represent certain products of the digestion of blood-cells and elements in the cytoplasm of the macrophages, together with a small portion of the disintegrating cytoplasm itself, abstracted from the cell. If the macrophages did not eat and digest blood elements of all kinds, there would be no platelets. Definite indications of the occurrence of iron were obtained by the Prussian-blue reaction. The form in which the iron was combined was almost as difficult to break down as is hemoglobin.

The explanation of the Kurloff bodies is that they are the result of an unsuccessful attempt on the part of the lymphocytes of the guinea-pig to digest red corpuscles. The nature of the alteration is quite different from that which occurs when hemoglobin is properly digested by macrophages, except that in this case also no pigment is produced. By the action of a ferment the hemoglobin is partially broken down. This is, however, the only share the lymphocyte takes in the production of the Kurloff body. The principal difference between the digestion of hemoglobin by the macrophages, and its alteration into a Kurloff body by the lymphocytes, is as follows: In the former case, the hemoglobin is metabolized entirely, the iron becoming incorporated into or associated with the cytoplasm in some complex protein combination. In the Kurloff body, the iron is at once split off from a considerable part of the protein substance which helped to constitute the hemoglobin; though even in the liquid content of the vacuole, the iron is more masked than free. The characteristic red-staining inclusions (after Giemsa) represent this remaining protein, which may itself be the product of some interaction between the original protein and the digestive ferment. The Kurloff bodies may occasionally occur free, being found in the peripheral blood and in spleen preparations, both smears and films. Ultimately these free bodies and their contents probably break up altogether and are dissipated in the blood.

(To be continued).

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**Effect of Saponin on Blood-Platelets and Their Regeneration.**

*J. Firket, Compt. rend. Soc. de biol., 85:730, Paris, Oct. 22, 1921.*

Myeloid metaplasia is peculiar in the spleens of rabbits injected with saponin. The various myeloid elements, myeloblasts, myelocytes, metamyelocytes, ancestral cells of the granulocytes, normoblasts, young erythrocytes and megalokaryocytes, occur in the pulp and large venous sinuses. The relative percentages are abnormal, megalokaryocytes being unusually abundant; megalokaryocytic metaplasia, rather than myeloid metaplasia, might be considered present. Megalokaryocytes enter the general circulation, reach the liver and are arrested in the hepatic or pulmonary capillaries. In sections they may be observed, deformed and reduced to a giant nucleus, polylobular and denuded of protoplasm. An attempt was made to learn whether there is a relation between the numerous megalokaryocytes and the action of saponin on the platelets. The experiments show that saponin produces lysis of the platelets still

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more energetic than its usual hemolysis. Observations tend to support the theory that platelets originate from megalokaryocytes, though they may also have another origin.

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**Clinical and Experimental Investigations on Blood-Platelets.**

*Erich Wittkower, Ztschr. f. d. ges. exper. Med., 25:73, Berlin, Oct. 14, 1921.*

Of all the theories advanced on the origin of blood-platelets, only those of Wright and of Schilling remain under discussion. Wright claims that they originate from megalokaryocytes, while Schilling traces their origin to normoblasts.

The methods of counting blood-platelets include (1) direct count (Olaf Thomsen), (2) indirect count (Fonio), and (3) enumeration in counting-chamber (Degkwitz).

In Thomsen's method, 4.5 c.c. venous blood are mixed in a centrifuge tube with 0.5 c.c. of a 10% solution of sodium citrate, shaken, and allowed to stand for an hour. The thrombocytes are found in a layer above the erythrocyte and leukocyte layers. With a leukocyte pipette a measured quantity is removed and the platelets are counted in a counting-chamber; the proportion of the citrated blood to the volume of blood-cells is determined. The disadvantages, besides the error due to adhesion to the glass, lie in the fact that this method is time-consuming, and it requires venipuncture and a large centrifuge. The advantages are that only one count is required and there is no contamination or admixture of tissue detritus with the material in the counting-chamber.

In the author's modification of Fonio's method, the tip of the finger is smeared with vaseline or paraffin and punctured with Franke's needle. A slide, carrying a drop of magnesium sulphate (14%) is held over the drop of blood on the finger-tip so as to immerse the blood in the magnesium sulphate solution. The mixture is stirred with a glass rod coated with paraffin, and is spread. Staining is done by the Giemsa-Romanowsky method. Fonio's method is practicable, but is somewhat inaccurate due to adhesion of the platelets to the slide. The count is derived by determining the proportion between platelets and erythrocytes. As the actual number of red cells may be determined in the counting-chamber, the actual number of platelets can readily be computed.

In Degkwitz's method, as modified by the author, the hand is immersed in hot water to cause hyperemia, and the finger-tip is punctured. The first drop is wiped away with gauze moistened in sodium citrate; the second drop is collected on a watch-glass coated with paraffin and containing 15-17 drops of a 3% citrate solution. After mixing well, the platelets and erythrocytes are counted with the Thoma-Zeiss apparatus, using objective No. 7 and a weak ocular for erythrocytes, a higher power for platelets.

**Morphology of Blood-Platelets:** (1) Most frequently these are medium-sized specimens, without a nucleus. (2) Rarely "giant platelets" are encountered. (3) Small forms are seen, whose relation to platelets is doubtful.

When the suspension of erythrocytes was incubated, in 4 out of 11 cases an increase of 1% in platelets could be found. The platelets cannot be considered as derived from erythrocytes, the positive results obtained being due, probably, to a division of platelets in peripheral blood.

Smears made from fresh red bone-marrow showed very few thrombocytes. No increase was observed during incubation. If, however, the marrow in the rabbit was irritated by daily increasing injections of electroferrol, the marrow of the femur, six days after the last injection, was soft and red, resembling raspberry jelly. Teased portions of this marrow, stained by the Giemsa method, showed numerous thrombocytes, and in addition, megalokaryocytes from which definite groups of platelets issued. Blood smears showed similar megalokaryocytes. The powerfully stimulating action of electroferrol on platelet production seems to recommend it for the therapy of thrombopenia. When the bone-marrow of patients was subjected to irradiation by x-rays, no noticeable alteration in the number of platelets occurred. But in the guinea-pig a marked diminution took place. In a severe case of Morbus werlhoffii, which had been demonstrated as essential thrombopenia, the hemorrhages resisted all therapeutic efforts, but ceased at once when the patient developed a febrile bronchopneumonia; at the same time the platelet count was considerably increased. When the temperature returned to normal, the platelet count decreased gradually, but the hemorrhages did not return. Any rise in temperature caused by the inoculation of fever-producing protein bodies or by protracted hot baths leads to an increase in the number of platelets, which, however, is of short duration and ends with a negative phase, as has been demonstrated by Degkwitz.

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Clinical Findings in Regard to Blood-Platelets.

*Benno Schilsky, Ztschr. f. klin. Med., 91:256, No. 3-6, Berlin, 1921.*

Only two theories of the origin of the blood-platelets are worthy of consideration. Wright's theory is that they originate from the megalokaryocytes of the bone-marrow, while the Schilling-Torgau theory assumes that they come from erythrocytes.

Wright's theory is based on (1) the fact that giant cells of the marrow have the same staining characteristics as platelets; (2) that the giant cells send processes into the venous spaces of the marrow, these processes consist of ectoplasm, have a central nucleus and closely resemble the platelets; (3) that platelets are found only in blood without nuclei but in which giant cells are found, and (4) that the clinical observations bear out the theory. Schilsky, after criticising this theory which has already been disputed by others, concludes that the named factors are not sufficient to prove that blood-platelets arise from giant cells.

On the other hand, the Schilling-Torgau view considers the platelets a modified form of the nuclei of erythrocytes. This conclusion is reached from the results obtained with Dominici fixation (rapid fixation) and examination of the blood, spleen and bone marrow. By this method the platelets are seen inside of the red cells or attached to them, the platelets appearing as distinctly circumscribed disks. It is also observed that platelets occur only in blood without nuclei, they are found only after the normoblasts have lost their nuclei, they contain nuclein and react toward the digestion test and acetic acid test like nuclear substance (Lilienfeld and Scherer), and they can be stained with nuclear stains. Finally Schilling claims to have seen the expulsion of platelets from erythrocytes under dark field illumination. The

change from normoblasts to red cells containing platelet-like nuclei has never been seen in the bone-marrow. Schilling assumes that this gap is filled in the same way as in the case of prespermatid nucleus and spermatozoa head, that is, by mitosis within the nuclei.

The author performed tests by the method of Schilling with normal and pathologic blood. The blood was taken from the vein of the arm, and treated as in Schilling's directions. The platelets were strikingly like cell nuclei and were found partly on the red cells and at times completely within them. Very rarely two platelets are associated with one red cell. In the pathological cases with platelet increase the platelets appear like typical pyknotic normoblast nuclei. Normal blood is less useful because the destruction or change in the nuclei has already progressed further than in pathologic blood; regeneration being marked in the latter. It may be considered that the platelets are not secondarily fixed on the red cells because there is almost always only one platelet to a red cell, they are never grouped and the characteristic picture is obtained only by rapid fixation, the slower methods of fixation showing that the platelets have already left the red cells. The author considers that the nuclear nature of the platelets is sufficiently established by the foregoing facts.

A clinical study was made on this basis. Fonio's method was used for enumeration because the limit of error does not exceed 10%, and if 2,000 erythrocytes are counted in the fields, the error is only 5%. The hemoglobin content was estimated by Sahli's method. The total count of platelets varied from 200,000 to 300,000 (in agreement with most authorities), the average being 259,000. The relative count varied from 40% to 60%. To exclude variations, the counts were made at the same hour each day.

1. *Central Changes.* (a) Excessive Production of Erythrocytes: This was studied in four cases of posthemorrhagic anemia. Regenerative hyperglobulia is accompanied by an increase in the platelets. A return to normal is first indicated by a diminution of the platelets as this life is much shorter than that of the red cells. At a certain period there are comparatively more erythrocytes than platelets; when regeneration decreases the number of platelets is less than the number of erythrocytes because more old and fewer young forms of red cells are in the blood.

The number of platelets is increased in malignant tumors, the number of red cells being normal or subnormal. The destruction of red cells is increased and the bone-marrow sends many more young forms into the circulation, a phenomenon which is also shown by the increased polychromasia. The abnormal elimination of the erythrocytes balances the increased regeneration so that the total number remains normal. Anemia and cachexia occur when the regeneration cannot keep pace with the destruction.

Reactive increases in the platelets as a result of increased destruction of red cells also occurs in pulmonary tuberculosis, chronic nephritis, tuberculous peritonitis and lymphogranuloma of the peripheral glands. Different statements are given as to the number of platelets in myelogenous leukemia. Some authors say the number is increased, others that it is normal and still others that it is subnormal. These differences may be explained by the condition of regeneration, which may cease in the later stages of erythrocyte destruction, or if the latter is very great it

may explain the increase in the number of platelets. Hereditary hemolytic anemia with marked polychromasia and increase in platelets is the purest type of anemia due to destruction of red cells. The marked increase of the platelets, and especially their close resemblance to nuclei, the presence of normoblasts and polychromasia in cases of Vaquez's polyglobulia are distinct signs of hyperactivity of the bone-marrow. The increase of the platelets in erythrocytosis (dyspnea and conditions of congestion) supports the supposition that there is an increased formation of cells rather than increased concentration of the blood. The author found a relative platelet count of 88% and 56% in two cases of uncompensated valvular heart lesions. Arsenic therapy increases the relative platelet count as well as the number of erythrocytes. Nägeli has demonstrated that during hunger, fewer red cells are destroyed and formed, and a mild erythrocytosis and a low platelet count should follow. The author cites 3 similar cases in which the erythrocytes numbered from 5.5 to 6.4 millions and the platelet value varied from 33% to 39%. As none of the persons were undernourished, the author assumes a special physiologic effort. In one case there was a tendency to marked bleeding after minor injuries and spontaneous bleeding from the gums, resembling hemophilia but with no familial predisposition. The platelet value was 68%, representing probably an hereditary hemorrhagic diathesis with disturbed function of the platelets.

(b) Decreased Production of Erythrocytes: The relative platelet count is greatly reduced during the aplastic stage of Biermer's pernicious anemia. The bone-marrow suddenly becomes hyperactive during the so-called blood crises. The platelet value rises (in one case from 26% to 80%) with the appearance of normoblasts, polychromasia and basophil granulation. The platelet value is always low in aplastic anemia without remissions. The manifestations of benzol poisoning can be explained in the same way, that is, by a disturbance of the bone-marrow. There is a reduction in the number of red cells, as low as 1,000,000, in cases of chronic poisoning. The same changes are seen after exposure to x-rays in cases of leukemic splenic tumors. The general bone-marrow insufficiency which leads to this aplastic anemia, is not due to exposure to the x-rays, but rather to stimulation of the spleen leading to a depression of the function of the bone-marrow. It is not only a splenogenous leukomyelotoxicosis affecting only the leukocyte function of the marrow, but it is a splenogenous myelotoxicosis affecting the marrow as a whole. Such splenogenous marrow depression is found in typhoid, malaria, syphilitic splenic tumor and in splenomesenteric lymphogranulomatosis. Hemorrhagic diathesis occurs in all of these when the inhibition of erythrocyte formation has reached a certain stage. All degrees of marrow injury are found in acute cases. The blood picture in the chronic intermittent form varies, depending on whether it represents the marrow degeneration stage or the intermission (regeneration). The chronic type also leads to aplastic anemia.

2. *Peripheral Changes.* Anaphylaxis: The blood-platelets are affected in anaphylactoid purpura from any type of infection. They clump and cause thrombi and hemorrhages in the internal organs. The platelets are reduced by the peripheral disturbance while the erythrocytes are reduced only after an external hemorrhage, but there is no connection between the latter and the number of platelets. Hemorrhagic attacks after injection of tuberculin may be classed as anaphylactoid

purpura. A decrease of platelets occurs after injection of tuberculin in healthy persons or in people with inactive tuberculosis, but only for a short time, a return to normal occurring after twenty-four hours. This recovery is slower in acute tuberculosis as it begins after forty-eight hours and the increase in the number occurs only after seventy-two hours.

On the basis of 400 of Degkwitz's cases, the author considers that the platelet count is decisive in determining, in conjunction with a positive Pirquet reaction, whether the tuberculosis is active. An analogous decrease of the platelets in the peripheral arts is anaphylactoid in nature and occurs in all infectious diseases. This may be an effect on the bone-marrow, either a stimulation or depression, depending on the nature and severity of the infection. The results can only be explained by the theory of Schilling, though conclusive proofs may be lacking.

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#### 1f. PATHOLOGY

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**Rudolf Virchow.**

*L. Aschoff, Deutsch. med. Wchnschr., 47:1185, Berlin, Oct. 6, 1921.*

Aschoff reviews the scientific and human qualities of Virchow. Virchow's greatness is due to his broad conception of the possibilities of pathology and his masterful analysis of physiologic and pathologic processes rather than to the way he solved individual problems. While he advocated scientific methods in medicine, as opposed to those of natural history and philosophy, he believed that medical science should aim at curing disease, and that scientific research should be only a tool for the accomplishment of this purpose. He believed that pathologic physiology has a fundamental importance in medical research. He recognized the possibility of a specific causative agent of many diseases long before bacteria were discovered. The development of cellular pathology was not Virchow's only service to medicine. He brought order into the empiric chaos in medicine at the beginning of the eighteenth century. He clearly recognized the disadvantages of a morphologic pathology. Virchow's conception of the nature of disease is valid even today. He viewed disease as life under conditions which were dangerous to the organism. He had modern conceptions of irritation, disease, degeneration and inflammation.

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**Rudolf Virchow and Constitutional Pathology.**

*R. Rössle, Münch. med. Wchnschr., 68:1274, Oct. 7, 1921.*

Morgagni first showed the pathologico-anatomic basis for considering disease due to local disturbances of health; Virchow completed Morgagni's idea by demonstrating that all normal and pathologic processes depend on the activity of the cell. His view is somewhat one-sided, since according to it disease results only from the manner in which different parts of the body react to the disease-producing stimulus; and the nature of the stimulus is regarded as of secondary importance. From our present standpoint, we note two peculiarities of Virchow's view of the life of the macroorganism, namely, disregard of the idea

of the human body as an organism, and, of the idea of the combat waged by this organism to preserve its existence. He forgot that life proceeds not alone from cell masses but also from the activity of non-vegetable structures and relations, from the blood and nervous system. Moreover, the cell is much more limited in its morphology and function than the general organism, on account of its specific differences in normal life and disease; the organism, because it is not merely the sum of various kinds of cells, reacts in a great number of ways to the stimuli of the external world. According to Virchow, causal pathogenesis is less important than formal, but, since he gave no false ideas of pathological conditions, his teaching easily stands against the storm of opinions based on bacteriologic discoveries which overvalue external factors. The great error of the localization theory in medicine, consists in the idea that the disease-entity must always be local. Etiology must always be considered in disease.

The author gives the following example of the difference between the constitutional, and the local, views: Rats whose food contains no fat develop corneal ulcer. If this partial starvation were not known and if the subjects were human, the physician who believed in the local disease theory would consider the ulcer autochthonous and treat the cornea in vain. Cure could be brought about only by a normal diet. The ulcer is constitutional, not local. The constitutional condition is an avitaminosis. The cause must be found instead of treating a "seat" of disease. Virchow was not ignorant of constitutional disease; he called a disease constitutional when the life processes departed for a considerable time from the normal, so that a general and essential change was induced in the organism. Constitution, in the medical sense, implies the entire personality of the individual, as formed by heredity and experience. General tendencies due to race, sex or age must be included in the medical estimate of pathogenesis from the very fact that they are factors fundamentally hereditary. The individual must be considered with reference to his heredity as well as his personality. Constitutional pathology is at present a question rather than an answer. So far it has been an aimless collection of morphologic or functional types of anomaly, named according to certain peculiarities; often there is no recognition of underlying pathogenesis, nor any discrimination between cause and effect, nor any distinction between essentials and non-essentials.

Every field of research requires a special method and none exists at present for constitutional pathology. So long as there is no special method, the methods of investigation used in other fields must be applied to the problems of individual constitution. The average values must first be found by anatomical study, by applying anthropological methods of computing weights and measurements in the living and the dead. A study of physiognomy must be made. The relation between the external appearance of the body and internal functions must be understood and to obtain this result a knowledge of the form for each organ is necessary. The gap between form and function must be bridged. A beginning has been made, in the pathology of the internal secretions, which is peculiarly the domain of constitutional conditions. But constitutional habit and tendencies can be understood only by going back to etiological sources. It may not be possible to separate the hereditary from the acquired conditions; an understanding of the individual can

be gained only by an accurate study of the average effects of external factors and a knowledge of hereditary taints and talents. Inherited disturbances depend in part on the period at which deviation from normal development began. The earlier the period at which it begins, the more strictly cellular is the pathology of the condition.

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**Virchow's Teaching in Regard to Cancer.**

*Carl Kaiserling, Deutsch. med. Wchnschr., 47:1191, Berlin, Oct. 6, 1921.*

Virchow believed that tumors were not heterologous tissue but were subject to the same laws as other tissues of the body. Even today the relation of the epithelial cells of cancer to the connective tissues is not understood. There are carcinomas which contain sarcomatous tissue and it is impossible to classify some tumors as sarcoma or carcinoma. Virchow's anatomic classification of tumors is still referred to. He divided tumors into 4 groups according to their origin and discussed their causes, malignancy or benignancy, and treatment. Many new points have been discovered since then and much has been changed; but Virchow's fundamental principles stand.

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**Observations on the Experiments of Belogolowi on Mechanics of Development and the Tumor Problem.**

*E. K. Piette, Berl. klin. Wchnschr., 58:1140, Sept. 19, 1921.*

In about 100 experiments the author has implanted homologous and heterologous embryos of rana, pelobates and bufo, at various stages of development, in the abdominal cavity and in the leg muscles of Rana esculenta, Pelobates fuscus, Bombinator igneus, Bufo viridis and Molge vulgaris. Necrosis, necrobiosis of the embryo and resorption always ensued. He never obtained the results reported by Belogolowi, viz., inhibition of further development, loss of power to form complexes, syncytial formation over the body-cavity, formation of structures resembling organs and formation of free, scattered and infiltrating "sarcoma-like" cells.

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**On the Transplantation of Rat Sarcoma in Adult Birds.**

*Y. Shirai, Japan Med. World, 1:15, Tokio, Oct. 15, 1921.*

Fujinaw's rat sarcoma was used for transplantation in pigeons by excising the tumor, cutting it into pieces about the size of a German millet, and inserting a piece through a very small trephine hole made over the middle portion of the left cerebral hemisphere, planting the piece 3-5 mm. deep into the brain substance. At the same time a piece of tumor tissue was planted subcutaneously in the same pigeon, for control. In 12 pigeons, 9 grafts showed positive growth, reaching the size of a small finger tip in twenty-four days and the size of a thumb tip in thirty-three days. The pigeons took squat position fourteen days after transplantation, with indisposition to move; many kept their eyes closed as symptoms progressed. Of the 3 pigeons in which growth was negative, one died the sixteenth day and the others were so wasted that they were killed. Examination at site of transplantation in these 3 showed a yellow tinged material about the size of a hemp seed,

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microscopically showing necrosis of the planted tumor tissue, surrounded by many foreign giant cells. There was a collection of lymph-cells in surrounding tissues, especially around blood-vessels. Subcutaneous plantation resulted negatively in all instances. In the positive growths, proliferation was by infiltration along the spaces around the blood-vessels, which were filled with nucleated red cells and a few white corpuscles. Reaction changes in surrounding tissues were not marked. The indurated part of tumor was composed mainly of spindle cells with a few oval, round or irregular shaped cells, and was markedly myxomatous. Soft part of transplant growth is identical with the original (round cell) sarcoma.

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**Digestive Activity of Mesenchyme. A. The Ehrlich Sarcoma Cells as Object.**

*Vera Danchakoff, Am. J. Anat., 29:431, Nov. 15, 1921.*

The purpose of the author's paper is to show that the phagocytic and digestive capacity of the mesenchymal syncytium or cellular reticulum of the adult chicken spleen is a direct and decisive factor in the destruction of the Ehrlich mouse sarcoma, and a factor of partial inhibition to the Crocker Fund mouse sarcoma 180, both of which grow vigorously when grafted alone upon the allantois of the chick embryo. In order to determine whether the mesenchymal syncytium of the adult spleen has a power over a living heterogenous cell, only such cells can be used as give an extensive growth when grafted upon the chick allantois. Rapidly growing transplantable tumors offer the most suitable material. The Ehrlich mouse sarcoma and the Crocker Fund mouse sarcoma 180 were chosen. The tissues were crushed by forcing them through a syringe with a sieve bottom. This procedure does not injure many of the cells nor even particles of tissue, but it loosens the texture of the tissue and seems to facilitate the access of cells and groups of cells into the allantois. Grafted simultaneously and in close contact, both spleen and tumor tissues grew. After six to seven days a large growth was usually found in the region of the graft, of which one part consists of splenic and the other of tumor tissue. Both tissues grew well at the periphery, except where they came into contact. Contact occurred at somewhat different stages after grafting, and a peculiar reaction invariably was developed in this region by the splenic mesenchyme, the reaction suggesting the phagocytic activity of a macrophage. The phagocyte in this case is not a single cell, but a mesenchymal syncytium with a common cytoplasm and numerous nuclei; the object of attack is the living cell of a mammalian tumor. As a result of this reaction the tumor stops growing at the place of contact with the splenic tissue, although it grows well in contact with the loose mesenchyme of the allantois.

In order to extend the mesenchymal reaction to the whole tumor graft, both tissues were brought into more intimate contact. Crushing splenic and tumor tissues together and mixing them carefully gave an intimate contact of the two kinds of cells. A preparation of such a mixture showed small particles of the tumor tissue enveloped by strands of splenic mesenchyme, the latter occasionally appearing in the form of small islands. Such a mixture of both tissues was used as a grafting material and the progress of the growth of these double grafts was

followed day by day. Encircling of the tumor cells is effected gradually and is easily followed microscopically. A rounding up of the tumor cell due to the contraction of its cytoplasm is brought about as soon as mesenchymal splenic cells closely approach it. Tumor cells with long processes at one side may be seen in preparations, while at the other side they are rounded up and in close apposition to a strand of mesenchymal plasmodium. The steadily and rapidly increasing number of tumor cells entirely encapsulated and cut off from the surrounding tissue demonstrates the inertness of the tumor cell when approached by adult splenic mesenchyme. The latter is the more active element and as a result the tumor cell is completely immobilized and surrounded by a kind of plasmodial capsule. The first detectable structural changes appear only in tumor cells already encapsulated. The gradual dissolution of the tumor cells is easily followed within the mesenchymal digestive zone. The author remarks that an analogy exists between the activity of the mesenchymal plasmodia against the tumor cells and the well-known digestive power of macrophages known to possess enzymes working in acid medium. Even if there were no evidence of enzymes in the mesenchymal cells or their derivatives, the study of the gradual disappearance of tumor cells within the mesenchymal capsules would furnish such evidence, the author believes.

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**Lipoids and Their Influence on Malignant Tumors.**

B. Sokoloff, *Compt. rend. Soc. de biol.*, 85:820, Paris, Nov. 5, 1921.

The vitality of malignant tissues is important. The author starts with the hypothesis, not yet verified, that fats and lipoids have a regulating action on tissue growth. Studies were made on solvents, especially ether. Sarcoma and carcinoma, before being inoculated into dogs and rats, were treated with solutions of ether (1, 2, 3 and 10:100). Control inoculations were made with tumors not treated in this way. Similar tests were made in vitro. *Results:* (1) Weak solutions of ether (1, 2 and 5:100) strongly stimulate the vitality of sarcomas and carcinomas, provided the action is brief (from one to twenty minutes). (2) There is an increase in the number of tumors which took, when inoculated, as well as in the intensity of growth, both of tumors and of cultures of sarcoma and carcinoma. (3) Dilutions of ether stronger than 5:100, or acting for a longer time on the transplant, diminish the virulence for culture, but increase the intensity of growth.

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**Occurrence of Tumor-Cells in the Circulating Blood.**

U. Quensel, *Upsala Läkaref. Förh.*, 36: No. 28, Stockholm, Sept. 1, 1921.

Formerly it was generally thought that every cancer cell which wandered from the primary tumor to another part of the body formed a new focus. It was also believed that cancer cells left behind after an operation caused recurrence of the disease. Recent investigations have, however, shown that the cancer cells are destroyed in the blood and lymphatic glands, without producing new tumors. The author has examined 50 patients with carcinoma and has found cancer cells in the circulating blood of 6. Four of the patients had cancer of the stomach, one (Sec. I—Page 210)

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cancer of the lungs and one a malignant hypernephroma. In all cases there were metastases in various organs, and the disease was in an advanced stage of development. Only a few cancer cells were found in the blood, except in the case of hypernephroma, in which there were a greater number of cells. In all cases in which cancer cells were found in the blood, the anatomic findings already indicated metastasis. The negative result in the other cases does not absolutely indicate that the blood was free from tumor cells, inasmuch as the demonstration of the cells is very difficult. The results, however, confirm the theory that cancer cells often enter the circulation and are able to exist in the blood. The findings were also in harmony with the theory that cancer cells are destroyed in the blood and may thus contribute to the occurrence of tumor cachexia.

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**The Histological Structure of a Case of Hemolymphangioma.**

*Paul Vigne, Bull. Soc. franç. de dermat. et de syph., Paris, No. 8, 1921, p. 417.*

In a recent report of a case of circumscribed lymphangioma attention was called to the presence of dilatations and new growth of lymphatic and blood capillaries. This association has been observed fairly frequently in tumors which are clinically diagnosed as lymphangiomas. The term "angiolymphangioma" seems therefore preferable. A case is described in which the dilatation of lymph-spaces and blood-vessels was very apparent.

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**Relationship of the Gonococcus to Amyloid Degeneration.**

*A. Buschke and E. Langer, Berl. klin. Wchnschr., 58:1136, Sept. 19, 1921.*

Efforts were made to induce amyloid changes by injection of a culture of gonococci and by injection of arthigon and gonargin. The result was never produced by injecting a vaccine; it was obtained with cultures only in a few cases as in Davidsohn's experiments. Success is therefore only a coincidence. Amyloid formation may be the effect of toxins of related proteins. The spleen appears to be the site of their formation. Micrococci morphologically related to gonococci may induce amyloid formation.

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**The Present Status of the Question of Inflammation.**

*Felix Marchand, Deutsch. med. Wchnschr., 47:1197, Berlin, Oct. 6, 1921.*

Inflammation is a complex pathologic process which accompanies many diseases. The 3 old cardinal symptoms, redness, heat and swelling, indicated that the process was due to circulatory changes in the inflamed part. In the middle of the last century it was thought to be due to congestion. Cellular pathology assumed that some external irritation causes a nutritive disturbance of the cells bringing about division of cells and the formation of young cells (pus bodies). Inflammatory hyperemia was considered a secondary phenomenon. With Cohnheim's

discovery of leukocytes, the vascular theory again gained ground. Cohnheim denied nutritive disturbances in the tissues, but these were later acknowledged by Ziegler and Thoma. Virchow denied that the nerves were involved in inflammation, as did Cohnheim and Samuel. Recently the neuropathologic theory of inflammation has again been admitted. The discovery of mitotic division of cell nuclei seemed to support Virchow's theory of active proliferation of tissue cells. This is not due to the direct action of the irritant but is a reactive phenomenon of the body against the injury to the tissues. As to the migration of leukocytes, the chemotactic theory was demonstrated by Wilhelm Pfeffer in motile plant cells. The present conception of inflammation is that it is a reactive process and serves to protect the body against injuries, especially those of an infectious nature. Aschoff suggests calling it "defense" instead of inflammation. He thinks parenchymatous changes are also reactive in nature, such as the slight degenerative changes of tubular nephritis for which F. Müller suggests the name of nephrosis. To include leukocytosis, fever and immunizing processes in the conception of general inflammation is only to increase the obscurity of the question. The neuropathologic theory has recently been much discussed. The disappearance of inflammation after anesthesia, which is explained as a local vasomotor reaction due to axon reflexes or direct reflexes between the skin and vessels, and the dilatation of vessels by products of metabolism, indicate that the capillaries are capable of functional dilatation, independent of the condition of the afferent arteries, and that irritation of sensory nerve-endings overcomes the normal tonus of the capillaries and causes dilatation. Inflammatory hyperemia apparently occurs first at the place which has been injured by toxins or similar substances. Afterward irritation of the dilators of the large vessels alternating with irritation of the constrictors extends centrally. At first there is irritative and later paralytic hyperemia, producing heat and redness. Ricker defines inflammation as a hyperemia due to irritation of the nerves and varying in form according to the degree of inflammation. Lymphocytes as well as neutrophil and eosinophil leukocytes migrate from the vessels. Polyblasts arise from lymphocytes. They are large lymphocytes which have taken up fat and resemble young fat cells. Unna's plasma cells play an important part in infections and new growths. A great part of these lymphocytes originate from the "wandering cells" of the mesenchyme, peculiar undifferentiated cells, which give rise to the small cell infiltration in chronic inflammations. Larger forms which correspond to the mononuclears of the blood (Mallory's endothelial leukocytes) and are very phagocytic, belong to the macrophages. The adventitious cells which are given off from the endothelial cells of the smaller vessels are also phagocytic. The new vessels which originate solely from vessels already present take part in inflammatory new growths (granulation tissue) as do also the fiber-forming connective tissue cells (fibroblasts), and the corresponding cells of the cornea, periosteum and perichondrium. Inflammation, therefore, means a series of local reaction processes in the blood-vessels and tissues which are caused by the action of various physical, chemical and infectious agents and lead to the formation of an inflammatory exudate, and in favorable cases to the overcoming of injury and therefore to recovery.

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**A Rapid Method of Preparing Tissues for Microscopic Examination.**

*Herman D. Melton, J. Lab. & Clin. Med., 7:112, Nov., 1921.*

By the method described, sections may be obtained in four or five hours that are as good as those usually prepared by slow elaborate methods. If the tissue is fresh it is cut into small blocks, about 5 mm. on the side. One or more of the blocks are covered with 4% formaldehyd in a test-tube and boiled over the flame for three minutes. The formaldehyd is poured off and the block, covered with tap water, is boiled for one minute, the water poured off, fresh water added and the boiling repeated twice, making three changes of water with one minute boiling for each. If the tissue has already been fixed in formaldehyd, the boiling in formaldehyd may be omitted. After the last boiling in water the block is covered with 95% alcohol, and is boiled cautiously three minutes in the flame; this is repeated three times or until thoroughly dehydrated, which, with experience, can be known from the appearance of the tissue. The block is covered with absolute alcohol in a wide-mouthed bottle, with air-tight stopper, and is kept at 55° for from  $\frac{1}{2}$  to 1 hour, depending on the size of the block. It is then placed in a solution of celloidin (6.5) in ether (60) and alcohol (40). The stopper is wired on, the block is heated for  $\frac{1}{2}$  hour at 55° C., and is put on ice to lower the temperature rapidly. When at room temperature the block is mounted, dried in the open air for from five to eight minutes, immersed in chloroform from twenty to forty minutes and sectioned.

(1f—13)

(1f—13)

**Microscopical Discoveries in Lethargic Encephalitis.**

*Guido Volpino and Giorgia Graziadei, Ann. d'igiene, 37:533, Rome, Sept., 1921.*

The authors have found special bodies and masses of material in lethargic encephalitis at the base of the brain. These masses are fixed in Zenker's fluid. There are slight capillary hemorrhages. In the white matter, when the sections are examined in iodin solution, these masses are seen in enormous quantities in the meshes formed by nerve-fibers. Some are small, scarcely measuring 15  $\mu$ ; others have a diameter of 80, 100 to 150  $\mu$ . They are stained a light yellow color by the iodin like the rest of the tissue. The small and middle-sized ones are round or oval or slightly polyhedral masses with blunt angles; the larger size are irregular in contour. They are often vacuolated. In the vacuoles there are small granulations stained yellow by the iodin. The substance which forms these figures is finely granular. The granules are small but very distinct and regular. In examining a section in glycerin the finely granular structure of these masses, is also very distinct. Some are so long that they give the impression of being swollen and degenerated, nerve fibers, or a substance compressed between the fibers and therefore assuming their form. Sometimes large blocks forming arches are found quite near the blood-vessels; it seems in this case that the walls of the vessel are transformed into this peculiar amorphous and granular substance. This substance does not swell; nor is it soluble in boiling water, ether or in acetone. It is not stained black by osmic acid. A very pale color is obtained with hematoxylin, and it stains fairly well with eosin. With eosin followed by a differential stain

with iodin solution the internal granulations are a little more apparent. With Mann's method a reddish tint is obtained quite different from the one seen in Negri bodies present in rabies. However, with the same method, some of the bodies found in encephalitis show internal figures as large as a nucleolus or even larger, of a deep blue-violet hue. These figures correspond to the vacuoles noted in the sections stained simply with hematoxylin, and with eosin.

The bodies of lethargic encephalitis are granular, more especially if they are examined in water or in glycerin, and they are not concentrically striped. The granulations which form these bodies have been stained electively by the use of Ziehl's fluid and by differentiation in absolute alcohol. In specimens stained in this way a large quantity of red granules, not more than  $2/10 \mu$ . in diameter, are seen within the masses. Few are larger than this. Many seem to be undergoing division; others seem to form little chains. They do not retain their color when stained by the Gram-Weigert method, preceded by immersion in 5% oxalic acid. The presence of these granulations differentiates this substance from simple hyalin substances, from the substance which is homogeneous in structure. The corpora flava of Siegert are hyalin, that is to say, homogeneous. They are not either lipoid or myelin substances. The substance is massed together in bodies or clumps, generally near the blood-vessels. These finely and regularly granular structures, which can be stained with Ziehl's fuchsin, should be taken into consideration in future studies of the causative agents of epidemic encephalitis.

(1f—14)

**Etiology of Herpes Febrilis.**

*A. Luger and E. Lauda, Ztschr. f. d. ges. exper. Med., 24:289, Berlin, Sept. 22, 1921.*

The authors confirm Löwenstein's finding that human herpes febrilis can be transmitted to the cornea of rabbits and guinea-pigs. The vesicles are washed with alcohol and a bit of their contents inoculated directly upon the cornea; or the contents, mixed with 2 c.c. physiologic salt solution, may be used for the inoculation. The cornea, anesthetized with 4% cocaine, was cross-hatched with the infected knife, the markings extending into the upper layer of the stratum proprium. Of 11 attempts at direct inoculation in rabbits all resulted in characteristic keratitis in from twenty to twenty-four hours. A suppurative conjunctivitis also appeared, gradually infiltrating the site of inoculation. The process was at its height on the third or fourth day. Ciliary injection was accompanied by small vesicles at the border, with discrete foci in the epithelium. The base of the vesicle was infiltrated and more opaque than the surrounding parts. The process was intense and produced diffuse corneal infiltration, iritis and suppurative conjunctivitis. Severe inflammation lasted nine or ten days; from the sixth to the tenth day superficial vascularization appeared in the form of pannus. Healing continued steadily, leaving a corneal cicatrix. In a few cases there were general even cerebral, symptoms. The authors confirm the results of Dörr and Vöchting, who obtained general symptoms by intravenous and subdural injection of the diluted contents of herpes vesicles.

A certain attenuation of the virus seems to accompany transfer to animals; with the same period of incubation, the duration of the  
(Sec. 1—Page 214)

severe period is reduced from nine or ten to six days. Indirect inoculation of the salt solution mixture gave results in rabbits corresponding to Löwenstein's. The results seem to depend on the length of time the mixture is kept before use and on the temperature, the virus appearing more active at lower temperature. Indirect inoculation is generally weaker than direct; the incubation time is lengthened, the duration and degree of the keratitis are less. Löwenstein's finding that inoculation of herpes into one eye confers immunity against new inoculation was confirmed in 10 of 12 tests on rabbits. Six other tests with doubtful material were not counted. The second inoculation was made 14 days, and 1½, 3, 4, 5½ and 6 months after the first. It could not be determined whether two abortive reactions were due to the interval, to idiosyncrasy, variation of inoculation material, or to effects of the first inoculation. One experiment was made as to the filtrability of the virus. Inoculation material, mixed with 2 c.c. physiologic salt solution was filtered through a Nordmayer-Berkefeld filter and was immediately afterward tested for bacteria. The filtrate was inoculated, forty minutes after obtaining the virus from the vesicle, into the right eye of a rabbit. The other eye was immediately inoculated with an unfiltered portion of the same dilution, kept at room temperature. The unfiltered dilution caused a typical mild herpes. The filtrate produced only slight clouding of the scarifications for two days; the result was either faintly abortive or entirely negative. A second inoculation with virus after three months showed both eyes immune; it might therefore be supposed that the filtrate had a specific effect, but Dörr has shown that unilateral inoculation produces immunity in both eyes.

The histologic changes of the cornea in inoculation herpes are similar to changes which Heidenhain has described as occurring in animal cells under the term "chromatolysis." The changes occur in the corneal epithelium and are characteristic of herpetic inoculation as was shown by 19 inoculations with human serum, horse serum, serum from blisters produced by burns, serum from a Pirquet reaction, pus, vaccine, impetigo contagiosa, and pure culture of pneumococci, none of which caused similar epithelial changes.

(1f—15)

(1f—15)

**The Protein Content of Exudates with Special Regard to Those Spontaneously Reabsorbed (Continued).**

*Giulio Natali, Riw. crit. di clin. med., 22:349, Florence, Oct. 25, 1921.*

Tables from observations on 8 cases demonstrate that after an exudate has been withdrawn artificially, it forms again with less density, less chlorids and less total albumin, particularly globulin. These modifications become more marked with repetitions of the process. But when an exudate is spontaneously reabsorbed, 2 results are possible: (1) The density and value of chlorids and total albumin may diminish, and of the single albuminoids, euserin and pseudoserin may diminish, while seroglobulin increases; that is, there is more resorption of the chlorids and serins than of water. Or (2) the exudate may become more dense, with a larger proportion of total albumin, which is reflected in all 3 proteins, but most noticeably in globulin; that is, there is more resorption of water than of saline and albuminoid bodies. The cause of this diversity of behavior is local, and is to be sought in physi-

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cal conditions proper to the exudate and even more to the serosa; there was no indication of general disturbances in any case. The presence of one or the other condition of resorption may give some indication as regards the prognosis. In cases of pleurisy where the exudate became denser, a certain amount of inflammatory condition of the pleura remained. A characteristic common to all the exudates studied was the greater increase of serum globulin than of serum albumin, and the consequent diminution of the protein quotient. Neither albumose nor peptone was found in the exudates nor in their successive modifications. Resorption is, therefore, not preceded by chemical modifications of proteins. These reenter the circulation unchanged in greater or less quantity according to the condition of the serosa. The examination of the protein content of exudates at intervals has a practical clinical value, because when there are no general disturbances, especially cardiac or renal, it may indicate the beginning of resorption, reinforcing clinical data.

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**SECTION 1—ANATOMY, PHYSIOLOGY AND  
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**SECTION 1. ANATOMY, PHYSIOLOGY AND  
BACTERIOLOGY**

**1a. ANATOMY AND PHYSIOLOGY**

(1a-71) (1a-71)  
**Table of Measurement of Cephalic and Craniometric Indexes.**  
*Edmond Bayle and Léon MacAuliffe, Bull. Acad. de méd., 86:421,  
Paris, Dec. 20, 1921.*

The authors have compiled a table by means of which the cephalic index corresponding to given maximal longitudinal and transverse measurements of the head may be read off at once. Applying this table to 257 records of anthropometric measurements of criminals originating from the French provinces they obtained results which correspond to other previous studies of the cephalic index of the French race. (The table is not given in this article.)

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(1a-72) (1a-72)  
**The Ligamentous Connection between the Occiput, Atlas and  
Axis.**

*Hecker, Compt. rend. Soc. de biol., 85:1149, Paris, Dec. 17, 1921.*  
There is considerable variation in the anatomy. The studies first made in man were extended to various species of mammals, such as the squirrel, ermine, cat, dog, chimpanzee. Care was taken to select animals whose upper vertebrae are similar. In man and the apes, the cervical vertebrae have short bodies, flattened by the weight of the head acting in the upright position. The lateral articulations are close and tight. In quadrupeds, the bodies of the corresponding vertebrae are elongated and the lateral articular capsules loose and flaccid. The ligamentous attachments are of 3 main types: (1) Simple, the transverse ligament being in fibrous syndesmosis with the axial tooth. This type occurs in the hedgehog. (2) The quadruped type. The vertebral bodies are long; the glenoid surfaces of the lateral articulations are oblique, almost vertical; the lateral articulations are lax; the axial tooth is suspended by a ligamentous system, highly developed, and preventing luxation in the longitudinal direction; the angles formed by the 2 lateral occipito-odontoid ligaments are relatively large but practically acute (in the cat, 84°, dog, 88°); the transverse ligament is simple; the lateral ligaments are poorly developed and only reinforce the articular capsules. (3) The type suited to the upright position. The vertebral bodies are short; the glenoid surfaces are almost horizontal; the principal movement is rotation; the lateral occipito-axial and Arnold's ligaments, which govern rotation and steady the head, are highly developed; the cruciform ligament is present; the angle of the occipito-odontoid ligaments is distinctly obtuse (in the lemur, 128°, chimpanzee, 146°, and the average human species, 155°-165°). Upright posture, shortness of the cervical vertebrae, horizontal glenoid surfaces, rotation and stability of the head, and angular measurements of the occipito-odontoid ligaments are in direct proportion to the development of the intraspinal, collateral ligaments, especially the lateral occipito-axial.

(1a-73)

The Different Forms and Origin of the Third Condyle of the Occipital Bone.

*L. Bolk, Anat. Anz., 54:335, Jena, Oct. 1, 1921.*

Bolk has tested the behavior of the posterior portion of the base of the skull with a material of 35,000 human skulls, including 2,000 skulls of children. He paid particular attention to the origin and form of the third condyle and noted the following results: There are 2 kinds of third condyle: (1) The most frequent is that in which articulation has formed between the condylus tertius, the back of the skull and the dens epistrophei. (2) More rarely a supernumerary articulating surface is found between the atlas and the skull. The autogenesis of the base of the human skull must be considered, in order that the varieties may be understood. In young embryos, just as in reptiles, the anterior surface of the dens articulates with the base of the skull. Also, the primary condyles of the occiput lie more ventrally and almost reach to the median line. As development continues, the anterior margin of the occipital foramen is removed from the dens and the surfaces of articulation between atlas and occiput wander further to one side, due to the fact that the primary condyles increase in size posteriorly and decrease anteriorly. Thus the primary condyles change to secondary ones by process of migration. In the skulls of children this process of migration is not yet complete, as opposition has taken place posteriorly but disconnection anteriorly has not, so that the condyles are longer than usual and reach further forward. The articulating surface can withdraw laterally to a further stage of development, but the medial ends of the primary condyles remain as margins; they may then develop into the basilar tubercles. These tubercles tend to enlarge and grow toward each other. There are cases where they unite. They may then form an odd (un)paired tuberculum, i. e. condylus tertius. This has a surface, facing posteriorly, which articulates with the dens epistrophei. Therefore the condylus tertius is not to be considered as a persistence of an autogenetic phase, but as a secondary, newly-acquired formation.

There is still another very rare form of the condylus tertius, which articulates with the dens. This is an extreme form, consisting of a pointed bone reaching from the anterior margin of the foramen magnum to the back. It originates from the ossification of the ligamentum apicis dentis. In those cases where the condylus tertius articulates with the atlas two groups can be differentiated: (a) As the transformation of the primary into the secondary condyle takes place, the medial end of the primary condyle can persist as an articulating surface on one side (condylus tertius); this is then separated from the secondary condyle by a long ledge. (b) During the process of migration the normal shortening of the anterior end may set in, and apposition be disturbed. This can occur when an abnormal course of the vertebral artery separates a portion of the articulating facette from the posterior end, thus producing the condylus tertius behind. All cases prove that monocondylia is secondary, while dicondylia is primary in the human. Even the homogeneous condyle of the reptile is a secondary formation and the autogenesis of these animals points to indications of this process.

(1a-74)

(1a-74)

**The Region of the Anterior Cerebrum of Anures.**

*H. Kuhlenbeck, Anat. Anz., 54:304, Jena, Sept. 15, 1921.*

In describing the architecture of the cerebrum of the anures, Kuhlenbeck made use of the phaneroglossa and the rana mugiens, bufo agua and other foreign varieties. He discusses the following: (1) olfactory lobe; (2) pallium; (3) septum; (4) basal nucleus. Proceeding from without inward, the following layers can be differentiated in the olfactory lobe: (a) the fila olfactoria; (b) the glomeruli, a and b, which constitute the *formatio bulbaris*; (c) zona mitralis; (d) zona molecularis; (e) zona granularis. C plus d plus e constitutes the *formatio lobaris*.

When compared with the model, progress is noted in so far as the zona mitralis has loosed itself from the periventricular cells and has migrated toward the periphery. In the olfactory lobe of the anures, we find a nucleus olfactorius anterior, a nucleus olf. posterior, and a nucleus intermedius adjacent to the *formatio lobaris*. The pallium is divided into three fields as in other amphibia: (a) the area medialis or primordium hippocampi, is variously developed in the different varieties, especially in the caudal portion of the hemisphere. (b) In the area dorsalis an advanced differentiation in the form of fragmentation of the basal layers is seen, and is especially marked in the bufo. This corticogenetico impulse is caused by different factors. (The neurites grow fast and press the cells toward the periphery, neurobiotaxis of Kappers, etc.). The layer of swarm-cells as well as the basal layer takes part in the formation of the cortex. (c) In the third field, the area lateralis, we can also differentiate 3 minor divisions: the pars dorsalis, media and ventralis. The pars lateralis may be homologous with the lateral, neopallear cortex-plate of the reptile, while the area dorsalis harbors a lateral, dorsal and medial cortex-portion. The area media is homologous with the median cortex-plate. (3) The septum is strongly developed. It begins in the mouth with the primordium hippocampi, pushes forward between the pallium and olfactory nucleus, swells up into a club-shaped tubercle in the region of the foramen Mouroi and gradually disappears behind the septum. We can differentiate the following parts of the septum: nucleus postolfactorius, medialis, cellulae septales, nucleus lateralis, pars fimbriata and nucleus medialis septi. At times fragmentation is found within the septal cells. (4) The nucleus basalis, which surrounds the angulus ventralis of the lateral ventricle shows two parts, the epistriate and the striate portion, and combines with the gray matter of the third ventricle at the level of the lamina terminalis.

(1a-75)

(1a-75)

**The Anthropology of the Sternum.**

*Walter Gersch, Anat. Anz., 54:347, Jena, Oct. 1, 1921.*

Gersch experimented with the behavior of the sternum in skeletons of 3 negroes, 3 Hereros, and one Hottentot child in order to turn the results of Lubosch's research on the human sternum to account according to race. Lubosch differentiates 2 types of sternum: (1) the primateoid, an ancient mammalian attribute; (2) the hominid type. The population of Europe has the sternum of the hominid type predominant, while the primateoid is found exclusively in all of the lower races examined.

(1a—76)

**The Diaphragmatic Vertebra and the Separation of the Dorsal and Lumbar Spinal Columns in Mammals.**

*H. Vallois, Compt. rend. Soc. de biol., 85:974, Paris, Nov. 26, 1921.*

Theoretically, the diaphragmatic vertebra is the one which marks the division between the dorsal and lumbar spinal columns, and it also marks the division between the anterior and posterior muscle systems which are concerned in locomotion on land. The anatomical characteristics which distinguish it are given, but nevertheless it is often quite difficult to distinguish this vertebra in mammals. This is because its distinctive characteristics are most marked in those animals which leap. When the spinal column is curved to form the arc of a circle just before the leap, the prediaphragmatic and postdiaphragmatic muscles act in opposite directions to extend it. In these animals, the diaphragmatic vertebra has a characteristic appearance but in the higher mammals this distinction is gradually lost.

(1a—77)

**Polyarticular Muscles.**

*H. von Baeyer, Anat. Anz., 54:289, Jena, Sept. 15, 1921.*

Outside of the true polyarticular muscles which spread over several joints, we have muscles with polyarticular tendons, and mixed polyarticular muscles in which individual portions spread over more articulations than the rest of the muscle. Furthermore, there are polyarticular muscles which are combined with mono-articular ones. Polyarticular muscles can cross over (sartorius muscle) and reach the extensor side from the flexor side of the bone, or may cross over facultatively, i. e., under certain circumstances. The flexor carpi radialis belongs in this class, crossing the axis of the forearm in pronation only.

The importance of polyarticular muscles first of all lies in the faculty of saving strength in certain movements, for instance, when a muscle passes over a number of joints. A substantial saving of power is attained when the source of power is centrally located. Another important function of polyarticular muscles (and this may be demonstrated with models), consists in locking the joints by power. Polyarticular muscle may also exert an action of transmission when the muscle is passively inefficient (at the limit of extensibility) or when it is in the state of static contraction. This latter condition is called tonus. We must differentiate between two kinds of tonus: (1) condition of stimulation in resting muscle; (2) the form of increased internal effort. The transmission of motion from one joint to another is beneficial for the completion of some movements, as for instance in the act of walking, in which flexion of the hip-joint is associated with flexion of the knee-joint and dorsal flexion of the foot. Also vice versa. The transferring muscles in this case are the rectus femoris, ischiocrural group and the gastrocnemius. Movements in which two or more joints move in a similar sense, for instance in flexion, are concomitant. Where one joint is flexed and another extended, the movements relating to the noncrossing polyarticular muscles, are contrary. While concomitant and contrary movements alternate in walking, the large joints of the leg move concomitantly in running.

The collective action of the muscles, so far as it is caused by the  
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(1a—77)

mechanical relations of the muscle, is their muscular coördination. This predominates in the spastic patient over the nervous coördination, for nervous coördination is weakened not only on account of disease, but the coupling of the joints by means of the hypertonic musculature is more intense than in the healthy individual. In tabes, the patient's muscle-tonus is diminished, and the concomitant movements do not act so well together, the powerful locking of the joints is deficient and the inhibition of movement in contrary motion is diminished on account of the lessened tonic insufficiency. Muscular coördination is disturbed, hence the wobbly gait. If we apply rubber-bands corresponding in course to the polyarticular muscles, the atactic gait is improved.

In artificial legs, the attachment of pulleys complying with the mechanism of the polyarticular muscles was beneficial. Thus the knowledge of the mechanism of the polyarticular muscles can be turned to practical account.

(1a—78)

(1a—78)

#### Anatomy and Pathology of the Autonomic Nervous System.

#### II. Morphology of the Peripheral Ganglia.

*Ernst Spiegel, Anat. Anz., 54:331, Jena, Oct. 1, 1921.*

The functional and pharmacodynamic contrast between the sympathetic and parasympathetic nerves leads us to think that morphologic differences can be noted in the structure of the distal trunk ganglia and peripheral ganglia. Spiegel has already examined the structure of the former in a preceding test, and compares the structure of the superior cervical and celiac ganglia with the ciliary ganglion, the subepicardially placed cells of the coronary plexus and the ganglia of Auerbach's and Meissner's plexus as the basis of these results. He found no variation in size nor structure of the nucleus and arrangement of Nissl-bodies, but noticeable differences in metabolism as evidenced by pigmentation, were observed. Two kinds of pigment were found in the ganglia of the distal nerve trunks and are evident in great number in the superior cervical ganglion of the aged. The ciliary ganglion is poor in pigment while the cells of the coronary plexus are free from it. Similar variations exist between the cells of the celiac plexus and Meissner's and Auerbach's plexus but these are probably not due to difference in age as no differences in degree of development could otherwise be proven. Further examinations will have to show whether these differences between portions of the sympathetic nervous system on one hand and the parasympathetic on the other, are decisive or not.

(1a—79)

(1a—79)

#### The Existence of an Interstitial Gland in the Testicles of Fish.

*R. Courrier, Compt. rend. Soc. de biol., 85:939, Paris, Nov. 17, 1921.*

Interstitial structures occur in *Gobius*, especially near the excretory duct and in *Hemichromis bimaculata*, the male being distinguishable from the female by red abdominal pigmentation. The structure of the resting differs from that of the functioning testicle in *Callionymus lyra*, which is remarkable for the adornment of the male at time of sexual activity. During sexual repose, the spermatic reservoirs are contracted; during sexual exercise, there are large interstitial spaces containing islands of cells, of dark nucleus and more or less abundant protoplasm.

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Their origin appears to be lymphoid. In *Girardinus reticulatus*, clearly dimorphic sexually, similar interstitial cells occur. Pigmented interstitial tissue occurs in *Cottus*. The testicle in certain individuals of species without interstitial tissue is of peculiar appearance, as reported by Champy, Policard, Aron and others. The interstitial tissue may be related to secondary sexual characters.

(1a—80)

**Review of Classification of Double Monsters, with Report of a Case.**

*Winifred Grant, Boston M. & S. J., 185:746, Dec. 22, 1921.*

The classification of double monsters by Wilder of Smith College is divided into 2 parts: (1) double monsters in which the component parts are equal to and symmetrically equivalent to one another; (2) double monsters in which the 2 components are equal to each other, but each one less than an entire individual. Under this class come monsters having 2 separate and equal heads and necks on a single trunk, which is normal or with some duplication at the shoulders, and with a single pair of arms. Examples previously reported are quoted. The one here described was born of a primipara, aged 28, whose maternal sister had had 4 children, each of whom developed multiple sclerosis on reaching puberty. The pregnancy was normal. Two photographs show that the monster had a perfect body and 2 perfect heads, one being slightly smaller than the other; it weighed about 8 lb. A roentgenogram showed double spine, double sets of ribs with an extra clavicle between the 2 heads. Doubling of heart or other viscera could not be demonstrated by x-rays.

(1a—81)

**Nerves and Nerve-Endings in the Human Ovary.**

*Yasokichi Agaki, Frankfurt Ztschrift f. Path., 26:165, No. 1, Wiesbaden, 1921.*

Researches were made on human ovaries acquired by operation and on ovaries of children who had died soon after birth, using stain after Ramon y Cajal and Bielschowsky's method. The nerves supply the musculature and blood-vessels and end between the stroma-cells. The interstitial gland contains an enormous mass of nerve-fibers; also in the hyperplastic internal theca of the marasmic follicle there are nerve-bundles in abundance, while in the theca of the normal follicle these are found only in small number. The correctness of the arrangement of nerve-bundles is most noticeable where the stroma-cells do not lie close together. The bundles end in points or in knobs. In the loose connective tissue at the hilus of the ovary there are cell-masses that are like ganglia. In the superficial layers of the true corpus luteum, sparse bundles are distinguishable, in the deeper layers their presence is uncertain; in the false corpus luteum they are never found.

(1a—82)

**Discontinuous Evolution of the Chondriome in the Ovum of *Sabellaria Alveolata* L.**

*E. Fauré-Fremiet, Compt. rend. Soc. de biol., 85:986, Paris, Nov. 26, 1921.*

Mitochondria are visible early in development, but concealed later by vitelline globules and fat droplets. By the action of gravity, the  
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cell contents separate into 3 layers. The lowest layer, comprising 2/5 of the ovum, contains the maturation spindle and vitelline granules; the middle layer consists of homogeneous matter; the upper is composed of fat. Staining of the mitochondria is difficult; after chromic fixation, stains of Altman and Galeotti, Khull, or modifications of these, may be used. The mitochondria appear as a fine, granular precipitate. If the mature oocyte be treated with alcohol, ether, chloroform, or two of these substances diluted in sea-water, concentrations up to 10% never produce vacuolization in the cytoplasm. The latter swells. The solvents are merged in the cytoplasm, the latter remaining dark to the ultramicroscope. If the action of the solvents is too prolonged, or if they are too concentrated, albuminoids precipitate. The fundamental substance appears to be an alkaline gel having some lipoid properties, and containing water, albuminoids, glycogen, etc. The ovum contains 6.8% lipoids, not including unsaponifiable substances, neutral fats, phosphatids and probably soaps. The cytoplasm may be considered as a complex system in equilibrium in 3 phases. The aqueous phase is continuous (homogeneous gel, containing albuminoids, glycogen and soaps); the 2 dispersion phases are constituted by fat globules and vitelline. Equilibrium is physical and chemical, solubilities differing markedly. A priori, the conditions permit the inference that mitochondrial constituents (phosphorated lipoids or compounds resembling lecithin-albumins) may be largely dissolved in the continuous phase. Such conditions are temporary, the composition of the cytoplasm varying during segmentation. The mitochondrial substances may separate during the dispersion phase which accompanies the usual morphological aspect of the chondriome.

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(1a—83)

**Variation in Sensitiveness of the Ovum of Sabellaria Alveolata L. to Fat Solvents.**

*E. Fauré-Fremiet, Compt. rend. Soc. de biol., 85:1051, Paris, Dec. 10, 1921.*

Mixtures of alcohol and ether or alcohol and chloroform, in sea-water, have given the best results. The eggs deposited by a large female in about one minute were washed and placed in a glass dish under a thin layer of sea-water. At regular intervals, a volume of liquid containing 200 to 250 ova was pipetted off and mixed with an equal volume of sea-water and one of the fat-solvent mixtures. A large drop was then placed on a slide and left for two to two and one-half hours in a warm moist-chamber. The number of ova cytolyzed was counted and estimated per 100. The result shows that the cytosis thus produced varies rhythmically with time. Five minutes after deposition, the ova are moderately sensitive to the solvents; the sensitiveness very soon increases, then falls to zero, then ascends to a remarkable maximum, occurring at the beginning of the metaphase of the first maturation-figure. The sensitiveness again decreases, reascends, and so on. If the ova are fertilized after an hour, the rhythm of the sensitiveness continues, but the maximum now occurs at the anaphase of each maturation-figure. The experiments show that the equilibrium of the lipoids of the two phases (soaps and esters) varies in a normal rhythm in the maturing ovum. If, instead of alcohol, ether or chloroform, a solvent-like acetone is used, superficial and reversible precipi-

tation of the cytoplasm occurs, but without any regular rhythm. The variations in the equilibrium of the fatty bodies of the ovum may modify its viscosity. The relation of the rhythmic viscosity-variation to the mitotic changes is one of cause and effect.

(1a—84)

**The Spermatozoon of Chetoptera.**

*M. Romieu, Compt. rend. Soc. de biol., 85:896, Paris, Nov. 17, 1921.*

Annelid zoosperms described by Retzius show the flagellum attached directly to the posterior pole. In chetoptera, a connection intervenes between head and flagellum. This connection is as wide as the head, prolonging the latter and showing no constriction. Spermatids and immature forms have been studied, in which stages the interpolated portion is absent. The head is ovoid or spherical, granules being grouped about the origin of the flagellum or dispersed in the cytoplasm. These spermatids are so similar to zoosperms described by Retzius, that possibly the latter has mistaken immature for mature forms. The granules around the origin of the flagellum stain; they unite to form a kind of crown about the posterior nuclear pole at the time of formation of the uniting or intervening portion. Retzius considers the granules derivatives of the accessory nucleus; but they stain by Regaud's method. Retzius' accessory nucleus is probably mitochondrial. It should not be hastily concluded that spermatozoa of polychetes have no middle-piece or mitochondrial structures.

(1a—85)

**Experimental Metamorphosis of Germ-Cell by Endocrines.**

*L. R. Groté, Deutsch. med. Wochenschr., 47:1461, Berlin, Dec. 1, 1921.*

The metamorphosis of the germ cell by endocrines is of the greatest importance in the study of constitution.

Known facts: creation of deformity in descendants after irradiation of semen of frogs (Hertwig), inferiority after alcoholic treatment of parents in guinea-pigs (Stockard), infantilism after extirpation of thymus in axolotl (Hart), etc.

Analogous conditions: children of alcoholics are often epileptic; the child of a syphilitic may suffer from infantilism without being syphilitic. Mongolism is possibly due to hypothyreosis of the pregnant mother (Stölzner).

The author fed 6 male and 6 female white mice of the same breed with thymus-extract by Abderhalden's method and in part with iodo-thyrin. One control-pair was fed at a time. Two of the animals fed with the iodo-thyrin died from overdosage; otherwise nothing remarkable happened. After feeding, copulation. Three weeks later all pairs gave birth to 4 to 7 young. Their average weight at birth was 2 gm. A marked retardation of growth was noted in the thymus animals. One of these died after seventy days without ever having been ill. Microscopic section showed no changes. The iodo-thyrin animals developed much better, 2 of them outgrowing the control-animals in the first weeks of life. This anomaly of growth affected all animals and was therefore not accidental.

(1a—84)

(1a-86)

Intranuclear Secretion in Epithelium of the Spermatic Pouch  
in the Queen Bee.

*R. Courrier, Compt. rend. Soc. de biol., 85:941, Paris, Nov. 17, 1921.*

Spermatozoa may live three to four years within the spermatic pouch of the queen bee. The epithelium of the reservoir forms a thick, syncytial layer, whose nuclei appear to have notable secretory activity. The nuclei are granular and contain numerous small caryosomes. Plasmatic nucleoli have not been found. Rapidly enlarging eosinophilic granules are formed at the expense of nuclear substance, probably chromatin. The granules originate at one pole of the nucleus. They even invade the nucleus, and as they grow the chromatin decreases. Migrating into the cytoplasm, they leave the nucleus reduced to the membrane or containing a little chromatin from which it may be reconstructed. These intranuclear and secretory granules are modified in the protoplasm, first showing vacuoles, then becoming liquefied; the products issue through the cellular membrane, coming into contact with the spermatozoa contained in the sac, the latter being thus nourished. The process strongly resembles possibilities in the function of the human epididymis. However, it is distinctly nuclear; the nucleus apparently contains substances necessary for nutrition of the sperm; the chondriome is thus shown to be not always indispensable for elaborating secretory granules. The histology is illustrated by a drawing.

(1a-87)

Reduction of Chromosomes by Cleavage through the Mitotic Chiasms.

*H. de Winiwarter, Compt. rend. Soc. de biol., 85:1109, Paris, Dec. 10, 1921.*

Janssens believes that the cleavage of the cell, and consequently the reduction in the number of chromosomes, occurs through the points where the mitotic threads appear to be twisted angularly. These points are called chiasms. The author's studies in insects develop objections to this theory. Cleavage accompanied by chiasm formation occurs less frequently than the appearance of other mechanisms. Instead of angular torsion and chiasms, double or multiple rings appear much more frequently, especially in insects and urodeles. Among mammals, chiasm formation occurs only in the rat. Simple rings are found in man. It may be that the appearance of torsion is produced by irregular thickenings or partial cleavages, and that there is no actual twisting of the chromatin. The author has noted the appearance of torsion occurring about chromosomes in the absence of conjugation, which fact is a very serious argument against Janssen's hypothesis, since it indicates that the appearance of chiasms has nothing to do with cell division and the transfer of hereditary characters. The author does not reject the possibility that the theory may be correct, but finds it doubtful. Formation of ova and spermatozoa, in man, rabbit and cat, shows a stage in which the chromatin is not double, but appears as a single large strand which breaks up into blocks and irregular masses. It then becomes arranged in 2 parallel, granular rows. The chromosomes rearrange themselves during this period. Reduction of the chromosomes and assumption of their new characters occur a long time before the

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final separation of the conjugated chromosomes and appearance of the chiasms or ring forms. The author considers that the paternal and maternal chromosomes are really mutually attracted and that altered polarity produces merely an appearance of repulsion. This explanation is in agreement with the "crossing over" idea, for groups, as well as individual particles, may undergo exchange. Naturally, the author does not pretend to solve the problem. The first division, tending to reduce the chromosomes, is readily explicable, but the second stage is still unexplained.

(1a—88)

**Sex Determination from the Eggs of Fowls.**

*R. Lienhart, Compt. rend. Soc. de biol., 85:1086, Paris, Dec. 10, 1921.*

The author advances the hypothesis that the average weight and the weight range of the egg are specific for each pure race of fowl. Within the weight range for a given pure race, the heavier eggs will produce males, the lighter eggs females. This theory has been tried out by many poultry raisers, a considerable number of whom report failure and criticize the principle. The author finds that the main difficulty lies in defining the term "pure race." No race can be considered pure, for the purposes of the theory, which has been recently crossed. Examples of pure races are the Houban, Brahma, Dorking, Leghorn, Bresse and Minorca fowls; the Faverolles, Mantes, Coucou and Malines breeds are mixed. The average egg weight and range for the Houdan breed are 55 gm. and 50-62 gm.; for the Brahma, 53 gm. and 48-60 gm.; for the Dorking, 62 gm. and 53-70 gm. The Faverolles represents a blending of all three breeds. The average egg weight is 60 gm., the range 50-70 gm.

(1a—89)

**The Caudate Intestine and the Bursa Fabricii of Bird Embryos.**

*Franz Keibel, Anat. Anz., 54:301, Jena, Sept. 15, 1921.*

As an answer to the supposition of Albert Fleischmann that the caudal appendage of the primitive urodaemum, the caudate intestine, is like the bursa Fabricii morphogenetically, Keibel emphasizes the fact that the bursa Fabricii of birds does not appear until after the disappearance of the caudate intestine. The standard plates published by Keibel and Abraham show that the caudate intestine is no longer discernible in a chicken 96 hours old, while the first signs of the bursa Fabricii become visible in the embryo when 5 days and 6 hours of age. Similar conditions were found in the melopsittacus undulatus and the duck. Without question the caudate intestine of the bird is homologous with the caudate intestine of mammals and has nothing to do with the development of the bursa Fabricii.

(1a—90)

**Morphogenesis of Long Bones Shown by Embryonal Grafts.**

*R. Simon and M. Aron, Compt. rend. Soc. de biol., 85:943, Paris, Nov. 17, 1921.*

Experiments were made on guinea-pigs. Bones obtained from fetuses of 55 to 95 mm. were grafted into subcutaneous cellular tissue  
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of the backs of adult animals as follows: (1) Entire bones in connection with those immediately above and below, parts of which were transplanted with them. (2) Entire bones, unconnected with neighboring bones or tissues. (3) Entire bones, connected by one extremity to the neighboring bone. (4) Fragments including the epiphysis, separated from its normal connections, and half the diaphysis. (5) Fragments of bone including the epiphysis connected with the neighboring bone and half of the diaphysis. (6) Diaphysis alone. The transplants all survived, adhered to the cellular tissue and became vascularized. Bones were removed in two to five weeks; in all cases, normal proportions were retained and their appearance was practically normal. In 3 cases (femur and humerus), the form was modified, presenting considerable concentric increase of the epiphyses, with increased length and thickening of the diaphysis; there was some flattening in the direction of pressure caused by the skin of the living animal. In 1 case, there was concentric increase in the free epiphysis and marked thickening of the diaphysis, the articulated epiphysis remaining normal. In all cases, there was concentric epiphyseal increase without modification of the adjacent portion of the diaphysis. In 1 case (diaphysis of the tibia only) there was no perceptible variation in thickness after one month. Inferences: If proliferation of the epiphyseal cartilage occurs in the direction opposite to that of normal development, periosteal growth is excessive. To show this effect, the diaphysis must preserve connection with the 2 epiphyses. Isolated, or connected with 1 epiphysis only, the diaphysis remains unmodified, even though the epiphysis proliferates. The diaphysis connected to both epiphyses, of which only one proliferates, develops abnormally. In order that the epiphyseal cartilage may preserve its regular mode of increase, the presence of the adjacent bones appears indispensable. Absence of notable modification of an isolated bone seems to be due to the stage of epiphyseal ossification, which was more advanced than in other cases at the time of grafting. Histological examination will be reported.

(1a—91)

**Vitality of Organisms.**

*B. Sokoloff, Compt. rend. Soc. de biol., 85:1100, Paris, Dec. 10, 1921.*

Regeneration and growth are generally considered to be related. If infusoria be divided down to from one-half to one one-hundredth of their volume, regeneration does not occur. However, the fragment can live for a certain time. Three conditions exist, namely, regeneration, unstable equilibrium and disintegration. These conditions may be modified in various ways. The author, using Bursaria, has studied the influence of inanition. Deprivation of nourishment for two to four days produces no change in the ability to regenerate, but this capacity rapidly declines if the same conditions are continued for four to seven days. If the original volume of the organism has been reduced only by half, the regeneration occurs with great difficulty. Fragments containing a large number of nuclear elements and relatively little protoplasm have but little vital activity. This relation (the so-called "nucleus-protoplasm relation") is highly important in the preservation of vitality. Inanition at first stimulates vital activity, then disturbs the nucleus-protoplasm relation and lowers vitality. Regeneration can occur after loss of the ability to grow.

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**Epithelial and Muscular Cicatrization.**

*A. Giroud, Arch. d'anat. micr., 18:55, Paris, Oct. 15, 1921.*

Experimental wounds were studied chiefly in worms (*Allobophora fetida*) and lampreys (*Petromyzon planeri*). Moreover, the latter bore sporocysts, which had produced open or cicatrizing lesions, upon which studies were also made. Restoration of epithelium occurs by displacement of normal epithelium, not by direct regeneration. Cicatrization is preceded by a variable period of delay. The epithelium becomes displaced about the wound in a zone whose depth is about equal to the radius of the wound. In simple epithelium, the cellular elements seem to separate out in groups. The only epithelial quality which they appear to retain is the ability to cover open surfaces which they encounter. Stratified epithelium becomes displaced in larger masses. Proliferation is a secondary process. It is localized at the margin of the wound, continues, for a short time only and occurs by mitosis. The destroyed specialized cells do not at once reappear. Changes occur in the epithelium contiguous to that which migrates. Cicatrization in muscle is derived from already existing muscular tissue. Myoblasts or sarcocytes constitute the mechanism. Only muscle tissue is concerned in the repair. The article is accompanied by numerous plates and an extensive bibliography.

(1a-93)

**A Revolving Contact-Maker to Stimulate at Any Required Frequency.**

*A. V. Hill, Am. J. Physiol., 58:494, Jan. 1, 1922.*

This device, which is illustrated in the article, consists of a simple revolving contact-maker composed of a circular plate of vulcanite with a number of phosphor-bronze strips inlaid into its circumference flush with the surface, on which a phosphor-bronze or stencil copper spring rubs as it revolves and so makes a number of short bursts of current which may be used for stimulation. The stand of the instrument consists of a heavy casting, and the vulcanite plate is mounted upon a spindle driven by a cone-pulley from a separate motor or from the shafting driving the drum, or from one of the pulleys on the drum itself. The battery is connected through the contact-maker to a pair of electrodes, which are used for stimulation of the tissue, so that each time a strip of phosphor-bronze touches the spring a current momentarily passes through the tissue and gives it a shock. The instrument can be driven at any required speed and the form of the current given by it as it revolves is very regular. The instrument can be used with an induction coil, being connected through the primary in the usual way, and the stimulating current taken from the secondary, but it is more satisfactory if used without an induction coil and directly connected to the electrodes.

(1a-94)

**Measurement of the Counterelectromotive Force of Polarization in Man.**

*A. Strohl, Compt. rend. Soc. de biol., 85:948, Paris, Nov. 17, 1921.*

The human body appears to offer considerable resistance to currents of very brief duration (.0001 second). This apparent resistance is ex-  
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plained as due to a counter electromotive force of polarization; the latter may exceed 10 volts. By means of a pendulum making 4 contacts, a current is passed through the body for a known time; immediately after, with a loss of time not exceeding some hundred-millionths seconds, the body is placed in opposition, aided by a sensitive galvanometer, with a known electromotive force, the duration of the opposition being measurable and very brief. In the tests, a large, nonpolarizable electrode was placed on the back, a similar, small electrode at the motor point of the common extensor. Resistance of 7,000 ohms was placed in series with the body; duration of the opposition, 0.0002 second; voltage, 20 volts. Seven periods of current-duration were recorded, varying progressively from 0.00018 to 3.0 seconds. The corresponding counter-electromotive force measured was 2 volts for 0.00018 second, progressively increasing to a peak of 9.7 volts (corresponding current-duration being 0.0018 second), then declining to 4 volts (corresponding current-duration 3.0 seconds). Passage of the current diminishes the bodily ability to generate counter-electromotive force. Values of the latter given above are approximate, polarization falling rapidly as soon as the current ceases. In one test, it was only one-fourth its maximum, after an interruption of 0.007 second, and only a few tenths of a volt after about 7 seconds. This report summarizes conditions of variation in apparent resistance of the human body, as thus far noted.

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**The Local Galvanic Reaction of the Skin.**

*U. Ebbecke, Pflüger's Arch. f. d. ges. Physiol., 190:230, Berlin, Oct. 4, 1921.*

It was determined by physical methods that the resistance of the human body is much less to an alternating current of high frequency than to direct current. The resistance to alternating current hardly changes if the skin is stimulated or irritated, whereas the resistance to direct current is greatly reduced by mechanical irritation, such as rubbing. The change in resistance occurs in the skin, but the stratum corneum or epidermis can be ruled out as the seat of this change. The local galvanic reaction remains strictly localized to the irritated surface and is not the result of some nervous factor, in contrast to the psychogalvanic or neurogalvanic reflex phenomenon. This is true of animal (frog, guinea-pig) skin as well as of human skin. Chemical (ammonia and acetic acid), and thermic irritation has the same effect as mechanical irritation. Chloroform, which causes an intense hyperemia, has practically no effect. Faradic irritation of the skin causes no distinct local galvanic reaction such as is produced by the continuous galvanic current. It is well known that the resistance of the body decreases after exposure to the direct current. The cause does not appear to be in a change of the circulation or blood.

This phenomenon may be explained on the basis that the results of electric and mechanical factors agree and are therefore of the same nature. The predominance of the mechanical factor is excluded and the change must be due to a combination of both factors. Prolonged exposure to the current causes a rapid reduction of the resistance at first, but this reduction becomes less and less, until it reaches a constant. The curve is reversed after the irritation is removed. The median degree of resistance is reached in about one-fifth of the time taken for full recovery.

The local vasomotor reaction is of the same type. Gärtner observed the same change in the cadaver but this does not discountenance the assumption of a physiologic phenomenon, as the cells of the skin react even ten days after death. (Walter). This explains the known changes in resistance in thyroid diseases. The decreased resistance in Basedow's disease, and the increased resistance in myxedema are expressions of increased or decreased metabolism. There is undoubtedly a relation between the skin currents and the changes in resistance, though this connection is not necessarily direct. Both are based on the rapid or slow, and more or less reversible changes in the permeability of the cell membranes. The permeability of cell membranes may be altered as a result of metabolic changes in the cell from the irritation. The change in the membrane may consist simply of altered composition or surface tension.

Currents of the skin and changes in the resistance are apparently symptoms of irritation. The author gives a physical interpretation of the electric changes which occur in 5 stages. The experiences show the possibility of attempting a determination of the function of the skin. This may be of practical importance for the dermatologist. The skin reacts in general diseases and might play an important part in the production of protective substances. It is possible that the epithelium exercises chemical as well as mechanical protection. The examination of the biologic activities of the skin may be of value in internal medicine.

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**Experimental Habituation or Immunity to Insolation or Heat.**

*C. Richet Jr., Compt. rend. Soc. de biol., 85:980, Paris, Nov. 26, 1921.*

Experimental conditions have been already described. No habituation is produced in mice heated for less than fifteen minutes, even though the heat is intense enough to kill half the mice tested. In mice subjected for twenty, forty or sixty minutes to temperature of 36° to 40° only, habituation results. With longer heating periods, habituation does not result before the twentieth day. There seems to be slight hypersensitivity during the first few days, probably because the heated mice are still affected when placed for the second time in the oven. From the twentieth to about the fortieth day, heated animals become more resistant than controls. Judging from 2 tests, habituation does not extend beyond the fiftieth day. If the resistance of the controls is represented by 100, that of the heated animals varies from 130 to 150. The habituation induced resembles immunity, but 5 attempts to transfer such possible immunity, by blood of heated animals, were not conclusive.

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**Physiology of the Selachian Endolymphatic Sac and Canal.**

*G. Portmann, Compt. rend. Soc. de biol., 85:1070, Paris, Dec. 10, 1921.*

The structure of selachians is especially well adapted for purposes of research. The studies here reported were made on *Leiobatis pastinaca*. The communication between the exterior and the endolymphatic pouch was closed by injection of paraffin or by superficial cauterization. Marked disturbances of equilibrium were produced by the pro-

cedure. The character of these disturbances has not yet been defined closely, but the importance of the endolymphatic structure in maintaining equilibrium is clearly evident. Viewed through the lateral wall of a glass aquarium, the normal fish swims in a horizontal plane; if treated as described, the fish cannot maintain this plane, but ascends or descends in an irregularly vertical direction. Viewed from above, the normal fish swims for long stretches in a straight line. The modified fish turns about and appears quite disoriented. There is great individual variation in the movements resulting from occlusion of the endolymphatic apparatus.

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**Variations in Attention during Rhythmic Stimulation of Sight, Hearing and Touch.**

*P. Dodel, Compt. rend. Soc. de biol., 85:1061, Paris, Dec. 10, 1921.*

Mosso's ergograph has been employed in these tests, mechanical fatigue being added to the fatigue produced by sensory reactions. The response to the stimuli is made by flexing the middle finger, to which is attached a weight of 2 kg. The registering cylinder is moved up vertically at each revolution, each record thus being made just above the preceding. Variations produced by stimulation of sight and touch are considerably greater than those occurring when the sense of hearing is stimulated. The tests were pushed until muscular fatigue was induced in the subject. The experiments suggest that the functions of the cerebral centers of the senses are specialized, hearing being passive, the other 2 senses more active. The auditory reactions being therefore less fatiguing, experiments of this nature should perhaps be based on the auditory sense to the exclusion of vision and touch.

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**The Effect of Repeated Rotation on the Duration of After-Nystagmus in the Rabbit.**

*S. S. Maxwell, Una Lucille Burke and Constance Reston, Am. J. Physiol., 58:432, Jan. 1, 1922.*

The authors studied the effect of daily rotation on the after-nystagmus in the rabbit. The observations were made on 10 animals, 5 of which were rotated with the head free and 5 with the head confined in a holder. In the experiments a specially designed revolving table (illustrated and described in the article) was used. The revolving apparatus was always stopped in the same way by means of a specially designed friction brake. In the cases reported, each rabbit was given 10 sets of 10 turns to the right and 10 turns to the left, 200 rotations in all, each day, Sundays excepted, until the end of the experiment. In carrying out the experiment, one observer supervised the rotation of the table and another manipulated the stop watch. At the instant the table stopped the watch was started and was stopped again when the nystagmus ceased. The authors' tabulated results show that the daily rotation of all these rabbits reduced, in some cases very markedly, the after-nystagmus. The authors attempted by the caloric test to discover the functional state of the labyrinth at the close of the series and they state that they have no reason to believe the animals were injured by the amount and rate of rotation to which they were subjected. They believe the results show that through habituation the organism was rendered less responsive.

(1a—100)

**Periodic Respiratory Plethysmographic Waves below a Constriction Which Abolishes Arterial Pulsation.**

*A. Mougeot and P. Petit, Compt. rend. Soc. de biol., 85:989, Paris, Nov. 26, 1921.*

Two ordinary sphygmomanometer cuffs are placed on the same arm, one above the other. In the distal cuff, connected to a Pachon-Boulitte oscillograph, pressure is secured equal to, or a little below, the arterial minimum. The proximal cuff is inflated to produce pressure equal to, or slightly above, the arterial maximum. The oscillographic bulb, connected to the distal cuff and receiving no cardiac impulse, registers curves which unmistakably show variations of volume in the limb. These variations correspond to the respiration. No recent works on physiology mention these respiratory waves. They are absent, or their amplitude is practically invisible, in subjects not dyspneic, at rest, and in quiet and superficial respiration. They are developed by exaggerated respiration and are ample and distinct in dyspneic subjects at rest. The volume of the limb in pulmonary tuberculosis, increases during inspiration, and declines during expiration. The waves are almost absolutely isochronic with phases of the respiratory curve, sometimes slightly retarded or advanced. Cardiopathic dyspnea produces inversion, and the synchronism with respiration is less distinct. In dyspnea, the waves are most distinct when pressure in the proximal cuff is 0.5 to 1.5 cm. Hg. above the effective pressure in the distal cuff. They disappear if the pressure is carried 4 or 5 cm. Hg. higher than that required to abolish pulsation. Rarely, ample waves have been noted under pressure in the proximal cuff equivalent to 10 cm. Hg. above the arresting pressure. These facts appear to have practical application; they indicate the exquisite sensitiveness of the Pachon instrument. It remains to be determined whether the impulses thus registered are due to incomplete arrest of arterial pulsation, or to vasomotor impulses transmitted from bulbar centers to arterioles and capillaries below completely occluded arteries.

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**Movement of the Blood in the Capillaries. II. Relation between the Velocity of the Current and the Pressure.**

*Adolf Basler, Pflüger's Arch. f. d. ges. Physiol., 190:212, Berlin, Oct. 4, 1921.*

Observation of the capillary circulation shows that extraneous causes modify the velocity of the current. The velocity is less after chilling of the skin and greater after warming. The resistance to the stream is a determining factor; this is increased if the lumen is decreased, and may be observed in the precapillary and postcapillary vessels as well as in the capillaries themselves. Simultaneous determination of the pressure and rapidity may show whether the contraction is venous or arterial. Narrowing of the arterial lumen must reduce the pressure while narrowing of the veins must raise the pressure. The velocity is reduced in both cases.

The velocity was measured by boring two holes in the microscope ocular close to the diaphragm, and passing a braid of three hairs through them. These braids were placed parallel with a capillary and the movement served as an indication of the velocity. A more exact determina-

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tion was obtained by employing a glass disk which could be rotated around the ocular. Several marks were made on this glass and the velocity was measured by these. The capillary pressure was measured with the capillary manometer.

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**The Contour of the Ventricular Volume Curves under Different Conditions.**

*Carl J. Wiggers and Louis N. Katz, Am. J. Physiol., 58:439, Jan. 1, 1922.*

By the use of a segment recorder which, in a closed system, has a vibration frequency of 20 per second, Wiggers and Katz found it was possible to record directly and accurately such portions of the systolic ejection and diastolic filling curves as were required for their study. They found in physical tests that such a volume recorder faithfully records such changes as are produced in the cardiometer without altering normal cardiac action. That the rates of ejection and filling were accurate, was further controlled by the fact that each change in ejection and filling rate corresponded precisely to changes in the aortic and auricular pressure curves. As a result of their studies the authors interpret the following changes in ejection and filling rates: In general, the rate of ejection is much greater during the phase designated as "maximum ejection," and is suddenly much reduced during the phase of "reduced ejection." During the phase of maximum ejection the rate of output is uniform only when arterial resistance is comparatively low. When it approaches or exceeds normal, the velocity of ejection changes in correspondence with optical aortic pressure curves. Diastolic filling under normal conditions of venous pressure proceeds as follows: Early in diastole, a rapid inflow takes place which accounts for 30 to 50% of the total filling. After this, the inflow is retarded and diastasis supervenes. The volume contributed by the succeeding auricular systole the authors found to range from 18 to 60% of the total filling under normal conditions.

Studies of optical curves interpreted with the aid of simultaneous pressure curves showed the following effects of increasing venous pressures by saline infusions. The ventricles respond with increasing strokes to increased venous return. Attending the increase in systolic discharge, the authors found an increase in diastolic volume and initial length but such changes were never dissociated from changes in initial intraventricular pressures. The authors observed that the duration of systolic ejection is progressively increased at constant heart rates and they state that it is in part through such systolic lengthening that a greater discharge becomes possible. Prolongation of systole is therefore a direct function of initial volume and initial pressure. Neither the systolic ejection nor diastolic filling curves are superimposable during increased venous return, but the rate of filling becomes more rapid in each of the consecutive phases of diastole and the velocity of ejection is also increased. The following reactions of the ventricles to increased resistance were established: The primary and constant effect of an increased arterial resistance was found to reduce the duration of systole, not to prolong it. In order to maintain a normal or augmented systolic discharge it is necessary for the velocity of ejection to increase. The abbreviation of systole incident to augmented arterial resistance may be

neutralized when a considerable increase in venous pressure attends the elevation of arterial resistance.

The authors remark that a study of the slow beats immediately following vagus stimulation shows that the progressive increase in duration of systolic ejection phases is not associated with a progressive lengthening of previous diastoles. It is associated with a progressive decrease in the ejection rate, i. e., a decrease in the gradient of the ejection curve. Since venous pressure increases during the course of vagus stimulation, the rate of filling increases in all phases of diastole, with the exception of the phase of auricular contraction during which there is less and less contribution as stimulation continues. As the ventricles do not empty to the same extent or with the same velocity, and since the diastolic filling rates alter during vagus stimulation, neither the systolic nor diastolic portions of the volume curves are superimposable, either on normal curves or on each other.

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**Have the Rhythmic Spontaneous Contractions of the Vessels a Demonstrable Influence on the Blood Current?**

*Kurt Wachholder, Pflüger's Arch. f. d. ges. Physiol., 190:222, Berlin, Oct. 4, 1921.*

The carotids of recently killed horses were attached to hooks, 10 cm. in length, after secure ligature of all the branches. The central end was fastened to a Mariotte flask and the peripheral end connected with a spring manometer. Sudden increase of the internal pressure causes slow contractions (after a latent period of at least eight seconds) and lasting not less than twenty seconds. Longer pieces of vessel showed spontaneous rhythmic contraction of at least thirty seconds' duration. The contraction ring in these cases remains stationary and shows no progression in the sense of a peristaltic wave. Similar contractions may be seen in the web of the frog's foot in which the capillary circulation is almost brought to a stand-still by contraction of the arteries. No external cause could be found for the rhythmic variations. These contractions have no influence in increasing the rapidity of circulation, as they last too long and do not progress in a wave. On the contrary, the contractions interfere with the capillary circulation.

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**Vasomotor Effects of Stimulating the Splanchnic Nerve in the Rabbit.**

*E. Gley and A. Quinquaud, Compt. rend. Soc. de biol., 85:1045, Paris, Dec. 10, 1921.*

Stimulation of the peripheral end of the splanchnic has appeared to indicate that the arterial pressure is raised in 1 stage in the rabbit, whereas in the dog or cat the elevation often occurs in 2 stages. The authors find that the results hitherto reported depended on the fact that a limited number of animals had been used and that these happened to show the reaction in one period. Of 42 rabbits recently studied, 30 gave the reaction in 1 stage, for 12 it occurred in 2 stages (primary elevation, fall and secondary elevation), as in the dog or cat. The reaction in rabbits is therefore not invariable.

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**Normal Chronaxia of Facial Muscles and Nerve in Man and Classification According to Chronaxia.**

*G. Bourguignon and A. Tupa, Compt. rend. Soc. de biol., 85:982, Paris, Nov. 26, 1921.*

Eight tests were made in normal subjects. The technic has been previously described. The reaction was obtained by stimulation of nerve and motor point of the muscle concerned, and differing chronaxia is obtainable without displacing the differential electrode. Superior and inferior branches of the facial nerve, and muscles so innervated, were studied. The average chronaxia for muscles innervated by the superior branch was 0.00058 second; the corrugator supercilii alone had low chronaxia (0.00024 to 0.00036 second), corresponding to that of the extensors and supinators of the forearm (0.00044 to 0.00065 second). Chronaxia for muscles innervated by the inferior branch of the facial was low, and similar to that of the corrugator supercilii and flexors and pronators of the forearm (inferior facial, 0.00030 second; forearm flexors and pronators, 0.00024 to 0.00036 second, innervation by median and ulnar nerves). Chronaxia is thus shown to accord with function. The levator muscles of the face correspond to the extensors of the limbs and have a high chronaxia; the depressors correspond to the flexors and have a low chronaxia.

(1a—106)

**A Respiratory Chamber for Large Domestic Animals.**

*A. Leroy, Bull. Soc. scient. d'hyg. aliment., 9:501, No. 8, Paris, 1921.*

Heretofore, there have been only two calorimetric chambers large enough for the study of the larger domestic animals, one at the Institute of Animal Nutrition of the Pennsylvania State College, the other at the German University of Bonn. Professor Benedict and his associates, of the Carnegie Foundation Nutrition Laboratory, aided by the personnel of the New Hampshire Experiment Station, have designed an economical respiration chamber, which the author describes. Details and plans are fully shown, accompanied by drawings. Typical calculations and tests are tabulated. Such a chamber has been installed at Durham, New Hampshire, under direction of the State University. Not including the technical apparatus, the cost was only \$150.00, or about 1,800 francs.

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**Hydrogen Ion Concentration as Regulator of the Depth of Breathing.**

*Alfred Fleisch, Pflüger's Arch. f. d. ges. Physiol., 190:270, Berlin, Oct. 4, 1921.*

Experiments were made on rabbits to corroborate the assumption that the pH in the blood has a regulating influence on the respiration. Solutions of primary sodium phosphate were slowly injected in the jugular vein; 10-15 c.c. of 0.167 gm. mol solution were given during one hour. The author measured the depth of ventilation, the carbonic acid tension, the pH of the arterial blood and the quantity of combined CO<sub>2</sub>. An increase of the pH of the arterial blood parallels an increase of pulmonary ventilation. Experiments determined that there was a reduction of CO<sub>2</sub> at the same time. This leads to the assumption that the pH influences the respiration in a regulatory way.

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**Types of Breathing in Various Sports.**

*W. Kohlrausch, Münch. med. Wochenschr., 68:1515, Nov. 25, 1921.*

In accordance with Kirchberg it is customary to distinguish between costal breathing and diaphragmatic breathing. Costal breathing includes: (1) chest breathing, during which the shoulders are drawn back and the chest arches forward; (2) lateral breathing, in which the arms are moved laterally; and (3) posterior breathing, during which the shoulders are moved forward, thus freeing the posterior costal region. In swimming (breast stroke) there is deep chest breathing, in connection with diaphragmatic breathing. The arm movements in this stroke correspond exactly with those used in breathing exercises; in fact, the sweep of the arms, with the shoulders held far back, brings about the natural form of chest breathing. In swimming on the back the posterior costal region is well inflated, and thus furnishes the impetus, so that the shoulders are drawn forward, hindering chest breathing.

Short-distance runners consume enormous amounts of oxygen during the period of exertion. The supply must be obtained by powerful thoracic movements, supplemented by the activity of the entire auxiliary breathing musculature. The type of breathing of long-distance runners is entirely different. They require a quiet, regular, slow breathing. The manner of running renders breathing with the entire pulmonary apparatus impossible, for the long-distance runner carries his body slightly inclined forward, and his arms are constantly being driven forward from behind. This produces a constant forward inclination of the shoulders, and, in the presence of slight kyphosis and wide intercostal spaces, leads to the posterior type of breathing.

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**Expenditure of Carbon Dioxide during Swimming.**

*A. Waller and G. De Decker, Compt. rend. Soc. de biol., 85:902, Paris, Nov. 17, 1921.*

Tests were made on a practiced swimmer whose vital capacity was 6.3 liters. First series: 50 m. at 1.562 meters per second; 100 m. at 1.282 m. per second; 100 m. at 1.250 m. per second; swimming on back, less than 1 m. per second. Cubic centimeters CO<sub>2</sub> per second expended in each test: 70, 53, 60, 35. Second series: 50 m. in 30 seconds; 100 m. in 80 seconds. Cubic centimeters CO<sub>2</sub> per second expended: 80 c.c.; 100.4 c.c.; expended during rest, 4.2 c.c. Subtracting 4.2 c.c. from the figure of the second test, the net expenditure appears to be 96 c.c. per second, or 533 calories, or 226.7 kilogrammeters. The equivalent is 1 H.P. for an engine, working the same time and giving one-third practical utility. Tables are included, showing more detailed analysis.

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**A Further Study of the Respiratory Processes in Mya Arenaria and Other Marine Mollusca.**

*J. B. Collip, J. Biol. Chem., 49:297, Dec., 1921.*

In a previous paper the author reached the tentative conclusion that *Mya arenaria* is a facultative anaërobic organism. Further investigation showed that various other bivalved forms and also certain of the gastropods continue to excrete, or to store and excrete carbon dioxid when the supply of oxygen in the medium is at a minimum. The object of this (Sec. 1—Page 236)

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investigation was to study quantitatively this apparent manifestation of anaërobiosis in such highly organized forms. The specimens to be studied were placed in fresh sea water in museum jars of known capacity and then sealed under water. After a definite period of time had elapsed, the jar was opened, the sea water was drained off, and the clams were removed to an open dish and allowed to drain further. The water which was thus collected was added to the larger fraction and the total volume determined. The clams were at once opened up and the interior of the shells freed of tissue. The entire contents of the shells were then drained, gentle pressure being used to expel the liquid portion. The fluid which was obtained in this manner was a mixture of true celomic fluid and of sea water trapped in the mantle cavities. The carbon dioxid content of the sea water used in the experiment was determined before and after, also the carbon dioxid content of the composite fluid expressed from the clam tissue was determined before on control specimens and afterward on the fluid obtained as described. The drained clam tissue was weighed. The volume of water displaced by the shells was determined and the volume displaced by the clams as a whole was obtained by subtracting from the volume capacity of the container used in the experiment the volume of water which was drained off from the clams when the experiment was concluded. Sufficient data were thus available to enable one to calculate the carbon dioxid production per 100 gm. wet drained tissue per hour. Collip has previously shown that the carbon dioxid produced by a clam when it is removed from its natural habitat may be in large part retained in the celomic fluid, becoming fixed as calcium bicarbonate. When one determines, therefore, the carbon dioxid content of the sea water or celomic fluid in an experiment, one is dealing, for the most part, with carbon dioxid fixed as bicarbonate. The carbon dioxid production is obtained by taking 50% of that present in the noted bicarbonate increase. This method for determining carbon dioxid production was checked up by determining the carbon dioxid excretion when clams were aerated with carbon dioxid-free nitrogen and the gas produced collected in standard baryta which was afterward titrated to phenolphthalein with standard acid. The results checked satisfactorily. No appreciable change was found in the pH of the celomic fluid of *Mya arenaria* or *venus* when they were kept for days immersed in paraffin oil, in a nitrogen atmosphere, in sea water in a sealed container, or simply exposed to atmospheric air. The pH for both normal and experimental specimens (determined colorimetrically using phenol red as indicator) was 7.8 to 7.9. Under all the experimental conditions imposed, the total carbon dioxid of the celomic fluid increased several fold. It is concluded that calcereous shelled mollusks, by virtue of being able to use the calcium reserves of the liver and the shell, exhibit the power to regulate their acid-base equilibrium with such precision that no change in the pH index is brought about even when they are subjected to most abnormal conditions. *Mya arenaria*, when placed under anaërobic conditions will survive for a period of time which is dependent upon the temperature. During this anaërobic period, carbon dioxid is produced at a uniform rate; this rate is accelerated by raising the temperature and depressed by lowering it. Glycogen disappears from the tissues during anaërobic periods. Potassium cyanid was found to depress the rate of carbon dioxid production under anaërobic conditions as well as to depress the oxygen consumption under normal circum-

stances. This points to the carbon dioxid production under anaërobic conditions as being due to a series of oxidations. The forms studied are unique in 2 respects: they can retain if necessary a large part of the carbon dioxid produced under aërobic or anaërobic conditions, by virtue of their ability to adjust their acid-base equilibrium at widely varying levels; they have a source of oxygen which is available in the tissues for metabolic needs during long period of oxygen insufficiency in the enveloping medium.

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**Stimulating Power for the Flow of Body Fluids. II. Osmotic Pressure of Albuminoids and Diuresis; Action of Caffein as a Diurétic.**

*Alexander Ellinger, Paul Heymann and Georg Klein, Arch. f. exper. Path. u. Pharmakol., 92:1, Leipzig, Oct. 11, 1921.*

In connection with the discussions of Fischer concerning edema, experiments were made to determine the influence of caffein and other purin derivatives upon the osmotic pressure of albuminoid plasma, as well as upon the diuresis caused by it. It was possible to exclude the action of increased blood pressure and hydremia, but a decision in regard to the point of attack of the caffein in the kidneys could not be reached. It is assumed that changes take place in water and that there is an osmosis between blood and tissue. At first a comparative irrigation of both legs of the frog preparation was performed according to Heymann and it was attempted to determine whether serum, pure and diluted with Ringer's solution and caffein, is able to bind fluids. This would become evident in a change of balance of liquid and weight. Outside of the necessary control tests in which edema had either been caused or not, in the corresponding anatomical part, the member was flushed out with serum, either with or without admixed caffein, in concentrations of 1:7,000, 1:28,000. In the leg flushed with caffein, not as much fluid passed from muscle to irrigating solution as in the leg treated without caffein. All test records showed that admixture of caffein diminished with aqueous absorptive power, i. e., osmotic pressure, of serum albumins. In general, less fluid passed into tissue where caffein had been admixed, than when not; this is explained by the fact that so much caffein passed from irrigating fluid to muscle, that the action upon the osmotic pressure of the albuminoid bodies in the tissue is more pronounced than upon the serum. The determination of caffein, by extraction with chloroform, and the determination of nitrogen, yielded figures which prove that in accordance with the amount of caffein acting upon osmotic pressure in serum or tissue, either the resorption of fluid from the tissue, or its transudation into the tissue is diminished. Through tests of the effect of caffein upon the osmosis in flushing with solutions of colloidal-free sugar or rubber, it was proved that a change in the permeability of the vessel wall plays no part in the action of caffein during osmosis. On the other hand, it was shown, in determining the speed of filtration in the ultrafilter, that a considerable acceleration took place. Even with weakest concentrations of caffein (1:56,000) it amounts to 20% in a 3 hours' test, and to 40% and more during the first two hours, with stronger concentrations. Similar to the irrigation test in the frog, we have here also the evidences of a diminished osmotic pressure of the serum through the caffein. Further tests with the solu-

tions of sugar and rubber exclude the probability that changes of membranes are out of the question as determining factors for acceleration of ultrafiltration of caffeine serum. By means of ultramicroscopic pictures, it was possible to observe the process of osmosis so well that it was easily determined which serum contained caffeine and which did not. It therefore appears that caffeine may owe its diuretic effect to an action on the capillary wall which causes extravasation. But the essential factor is probably the physical and chemical change in the albumin of the blood, as the effect of the caffeine makes itself felt upon their osmotic pressure in the glomeruli first of all. Water, or salt solution, which has been held in combination until then, becomes free and is more easily squeezed out.

In this manner the diminished retrograde resorption of Hans Mayer becomes intelligible. It is not necessary to suppose that caffeine possesses a stimulating action on secretion of renal epithelium. Outside of the kidney, the effect of the caffeine depends upon the amount passed into the tissue, and upon the pressure of osmosis present in the tissues. Transudation of blood into the tissue is restricted by caffeine, as a rule. This is favorable in preëdema cases. However, when the osmotic pressure in serum is increased by  $\text{CO}_2$ , the action of caffeine is unable to facilitate the drainage from tissue to blood, and may fail entirely. The behavior of osmotic pressure gives a sufficient explanation for caffeine fatigue, and for the nonappearance of marked diuresis in rabbits and dogs which have received dry nourishment only. In both cases, diminishing the supernormal osmotic pressure, caused by an increase of volume of water in tissue, suffices to reëstablish caffeine diuresis.

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#### Influence of the Digestion on Urinary Elimination.

*P. Violle, Compt. rend. Soc. de biol., 85:1146, Paris, Dec. 17, 1921.*

Previous experiments have been complicated by not eliminating the effect of liquids, which largely increase diuresis. The conditions observed in this test were as follows: The last meal preceding the test is taken at 7 o'clock in the evening. The bladder is then voided; afterward a regular quantity of water is taken during the test, namely, 25 gm. every fifteen minutes. No liquid is added during meals, which are limited to solid food. The subject remains on his back during the experiment, the bladder being emptied every hour. The quantity of urine is clearly diminished. Before the noonday meal, the average quantity passed is 150 gm. During the four hours following, the quantity falls to 45 gm., rising to the former quantity and again falling after the evening meal. The fall after meals is characteristic. The quantity of chlorids is proportional to the water eliminated. The urea curve approximates that of the chlorids, with smaller variations. The portal blood pressure is similarly affected, rising to 16-24 mm. Hg. during digestion, whereas the figure for other periods is 7 to 14 mm. The increased blood pressure explains the opsiuria, which may be properly termed "digestive opsiuria."

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#### Peristalsis of the Human Small Intestine.

*G. Ganter, Münch. med. Wchnschr., 68:1447, Nov. 11, 1921.*

Ganter describes a test to determine the pharmacological behavior of the small intestine.

By means of a piece of glass coupling, a part of a rubber condom is attached to one end of a thin rubber tube about 1 m. long, in such a fashion as to form a narrow rubber ring at right angles to the tube. The interior of this ring communicates with the lumen of the tube. A T-tube is attached to the other end of the rubber tube; one end of the T-tube is connected with a Marey's capsule, while the other terminates in another system of tubes. This second system consists of a water manometer and 2 communicating bottles partly filled with water. By raising or lowering the bottles, the pressure in the entire system can be varied at will. The patient swallows the end with the rubber ring. After 60-70 cm. have passed beyond the line of the teeth, the other end is attached to the ear of the patient, who reclines on the right side. After a shorter or longer time, often after an hour, the patient is conscious of a traction from within. This indicates that the tube has entered the duodenum, and its outer end is now connected with the pressure and registering systems. The pressure produced by raising one of the bottles can be read off on the manometer; it is transmitted to the rubber ring and causes it to dilate. At the same time, the pressure is registered on the kymograph by means of the Marey capsule. When a definite pressure is exerted on the inner surface of the small intestine, rhythmic peristaltic contractions are produced, which continue as long as the pressure exceeds the lower limit. If the latter has been reached, peristaltic contractions cease. The average limit of pressure is 15 cm. water.

This apparatus serves to test a number of points concerning the small intestine: interdependence of the size and frequency of contraction and the amount of pressure; fatigue of the intestinal wall after continued contraction; peristaltic wave in the intestinal tube; action of laxatives; local effect of drugs.

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**Cholin as a Hormone of Intestinal Movements. III. Action of Cholin on the Intestine as Compared with Several Organic Acids.**

*J. W. Le Heux, Pflüger's Arch. f. d. ges. Physiol., 190:280, Berlin, Oct. 4, 1921.*

As free diffused cholin is present in large quantities in the excised small intestine, it is certain that it stimulates Auerbach's plexus and the automatic movements of the bowel. The variable effect of atropin on the intestine may be explained on the basis of the quantity of cholin present in the intestinal wall. Experiments were made to determine if cholin affected the influence of other substances on the movements of the intestine. Neukirch and Rona found that even small quantities of sodium salts of fatty acids affected isolated segments of bowel. This stimulation may be due to the formation of cholin esters, in which event, cholin esters are even more effective than cholin. It should also be shown that the salts of fatty acids are not more effective if the cholin is washed out before the new cholin appears in the bowel. The assumption of the effect of cholin in the stimulation by the salts of fatty acids must be substantiated by abolishing the stimulation by atropin.

Experiments on excised rabbit's intestine proved the truth of the assumption. The following acids produced effects in the order mentioned: acetic acid, butyric acid, propionic acid, formic acid, isovalerianic acid, benzoic acid and succinic acid. The cholin esters follow the same

order. Acetylcholin is about 1,000 times as effective as succinic ester.

The stimulation by the salts of fatty acids may be explained by the presence of cholin which is capable of combining with the acids to form esters and of producing the effect of a synthetic ferment. Possibly the same is true of the sugars which stimulate intestinal movements by the formation of an ester during the breaking down of the sugar to pyroracemic acid.

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**Cholin as a Hormone of Intestinal Movements. IV. Influence of Cholin on the Normal Movements of the Stomach and Intestine.**

*J. W. Le Heux, Pflüger's Arch. f. d. ges. Physiol., 190:301, Berlin, Oct. 4, 1921.*

Cats were starved for twenty-four hours and then given 25 c.c. of mashed potatoes with 10 gm. barium sulphate. They were tied down and roentgenographed one-fourth or one-half hour later. The gastric movements were distinctly influenced after injection of 4-10 mg. cholin hydrochlorate. The peristaltic waves of the pyloric antrum increased in depth and number. There was a quicker emptying of the stomach and a more rapid passage of the contents into the small intestine. The pendulum movement of the small intestine increased after injection of cholin and the colon was filled more quickly than normal. The small intestine was empty in half the normal emptying time. Stimulation of the small bowel could not be observed but the contents passed more rapidly in the terminal portions of the bowel though not resembling the effect of cathartics. Increase of the cholin content of the body increases the movements of the stomach and intestines for hours. There are no spasms nor any abnormal movement—only a more rapid emptying of the intestines.

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**Action Currents in Stomach and Intestine.**

*Walter C. Alvarez and Lucille J. Mahoney, Am. J. Physiol., 58:476, Jan. 1, 1922.*

The authors made these observations on the stomachs and intestines of dogs, cats and rabbits opened under ether or urethane anesthesia. To expose the stomach a transverse incision is recommended, running along the lower edge of the ribs from one side to the other. Rabbits show better peristalsis if the cord is destroyed from the lumbar to the mid-scapular region, but with dogs and cats such pithing was found to be unnecessary. After applying the electrodes, the wound is closed as far as possible and moist gauze is used to protect the viscera from drying. In the experiments the animals were kept warm by an electric pad. Dogs were found to exhibit the most active gastric peristalsis. Rabbits are better suited for studies on the intestine. The authors' records were made by directing the beam of light from the galvanometer mirrors through the slit of a camera on to a revolving drum covered with bromid paper. The time record was obtained by fastening a little mirror to the armature of a signal magnet so devised that the mirror tilted when a current was sent in by way of the clock. Nine of the electrograms obtained by the authors are shown in the article. They reveal, among other things, some evidence of gradients of potential along the stomach

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from cardia to pylorus and along the bowel from duodenum to colon. Orad regions are negative to caudad ones and, in the rabbit, the stomach and cecum, full of digesting food, were found by the authors to be negative to other parts of the tract. The electro-enterograms obtained by attaching electrodes to various parts of the stomach and bowel resembled the mechanograms of the rhythmic contractions of bits of muscle excised from these parts. In the stomach the authors found a negative variation traveled from the cardiac region to the pylorus every twelve to thirty seconds. The cardiac region showed from 6 to 20 deflections in a minute, superimposed sometimes upon other large tone-like changes which were synchronous with the gastric waves. Marked electrical changes were found in the duodenum following the arrival of gastric waves at the pylorus.

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**Michrochemical Reactions of the Bile.**

*M. Aron, Compt. rend. Soc. de biol., 85:1154, Paris, Dec. 17, 1921.*

Liver and bile of the horse, ox, sheep, calf and pig were examined. Groups of basophil granules are constantly present in the liver of these animals; they appear about the biliary capillaries and may be detected in the bile. Their reactions indicate that they are alkaline or earthy carbonates or phosphates, and probably acid salts. They indicate the intensity of biliary excretion by the hepatic cells. They are increased during digestion, diminished by fasting. In the horse, sheep and ox, only, a fine, granular, yellowish pigment is present during digestion. It is best shown by fixing with absolute alcohol and staining with Giemsa or toluidin blue. The pigment is also reduced by fasting, and is probably only temporary. Chemically, it does not correspond to bilirubin and it can scarcely represent an intermediate product. It gives no iron reaction. It probably results from the diet peculiar to herbivora.

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**The Electric Endosmosis of the Hepatic Cells of the White Rat.**

*E. Fauré-Fremiet and P. Girard, Compt. rend. Soc. de biol., 85:1140, Paris, Dec. 17, 1921.*

By using various solutions, the contents of the hepatic cells may be rendered more dilute or more concentrated at will, the result depending upon the degree of ionization employed. Osmotic processes of living cells are not the same as those occurring in ordinary laboratory preparations. The question which is especially interesting is, whether the cells in the walls of the cellular interstices also share in the endosmotic effect. This is not the case in certain tissues, such as the cornea or conjunctiva. The liver cells are especially adapted to such a study. The cathode is placed on the body of the animal, the anode in the solution applied to the anterior surface of the lobe which is examined. Endosmosis, indicating by swelling, is produced only by a slight increase of free hydrogen ions or neutral salts of polyvalent cations. The animal is subsequently killed and the cells examined microscopically. The changes induced by this means gradually disappear. The method will permit further study of penetration into the cell by various ions.

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**Nutrition Experiments on a Dog with Fistula.**

*K. A. Zahn, Jahrb. f. Kinderhik., 96:245, Berlin, Nov., 1921.*

By the formation of fistulas in various parts of the gastro-intestinal tract of a dog, observations of the digestive process can be made, such as could never be made in man. A valuable fact is that the digestive processes in man and dog are remarkably alike. To eliminate errors, it is necessary to reintroduce the intestinal content so as not to disturb the reflex action of gastric and intestinal digestion; also the experiments must be made on the same animal and with the same nourishment. The author had 3 dogs with duodenal fistula, and 1 dog with a fistula in the middle of the small intestine. By exactly determining the time of each digestion quantity, which was rejected through the fistula, it was possible to determine the time for rejection of the total amount, the total amount of secretions, in enteric fistula the manner of emptying of the stomach, and the secretions of bile and pancreatic juices. Experiments gave the following result: (1) Under normal conditions in a dog with duodenal fistula, the process of secretions was not remarkably different for whole milk, buttermilk and skim-milk. (2) Under pathological conditions, that is, in an animal so affected by heat that a considerable reduction of hydrochloric acid in the gastric juice occurred, there was an abnormally rapid rejection of whole milk and skim-milk as well as neutralized buttermilk, while there was no change from the normal in buttermilk with the usual acid content or in skim-milk to which had been added lactic acid. (3) Therefore, the lactic acid content of buttermilk under the given pathological conditions, is of great importance in the course of gastric and intestinal digestion. (4) A simple addition of butter or cream to a mixture of milk-water-sugar, brings about an abnormal digestive process, in contrast to that of buttermeal nourishment. (5) The increasing amount of extractives, which stimulate the chemical gastric secretions, are also present in sufficient quantity in German dried whole milk. (6) Extract of malt preparations do not contain similar extractives. It is very insufficiently absorbed in the small intestine of the dog. (7) Addition of plasmon to skim-milk has the same effect on gastric digestion as rubio. Therefore it is necessary to presume analogous extractives in Daucus extract as in plasmon.

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**Animal Calorimetry. XVIII. The Behavior of Various Intermediary Metabolites upon the Heat Production.**

*Graham Lusk, J. Biol. Chem., 49:453, Dec., 1921.*

The author desired to investigate the comparative behavior of various simple substances, such as acetic, glycocollic, lactic, and hydrochloric acids; the behavior of glycine after neutralization with sodium bicarbonate, of sodium lactate and sodium glycocollate, and of sodium bicarbonate itself. The object was to discover to what extent the acidic radicle was a dominant factor influencing metabolism.

A dog was given the "standard diet" at 5 p. m. the day before the experiment and also regularly throughout the entire period of experimentation. The basal metabolism was determined about eighteen hours after the ingestion of this maintenance diet. Since strong solutions of acetic acid were vomited by the dog, only small quantities could be administered to the animal. As noted in the previous paper by the author, (Sec. 1—Page 243)

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it was found possible to administer materials like lactic acid in a solution containing 2.5 gm. of Liebig's extract of beef warmed to a temperature of 38° C. For the reason of the presence of Liebig's extract in the diet, the protein metabolism throughout the whole series of experiments was estimated on the basis of a urinary nitrogen elimination of 0.132 gm. per hour, as was determined for the basal metabolism of the dog employed. The figures given in the article represent in general the measurements of the metabolism obtained during the second and third hours after administering the substances. The author found that the ingestion of 400 c.c. of a broth containing 2.5 gm. of Liebig's extract of beef increased the heat production of a dog from a basal level of 16.1 calories by 0.5 calory per hour. The addition of 8 gm. of sodium bicarbonate to the broth caused no further change in the metabolism. The addition of 3 gm. of acetic acid to the broth causes an increase of 3.1 calories per hour. Lactic acid, 4.8 gm. given as before, raised the basal metabolism by 2.7 calories. With 10 gm. of sodium lactate the heat production increased only 1.4 calories per hour, possibly because the alkali favored its transformation into glycogen. Glycocollic acid, 7.6 gm., with twice the number of potential hydrogen ions contained in it that were present in 3 gm. of acetic acid, increased the metabolism by 1.5 calories or less than half that effected by acetic acid. A like quantity given as glycocollate of sodium increased the metabolism 0.88 calory. Hydrochloric acid, 1.8 gm., caused the metabolism to increase 1.6 calories per hour. Glycin, 9.55 gm., containing 20 calories and neutralized with sodium bicarbonate, caused the heat production to rise 5.3 calories per hour. Neutralization therefore did not avail to reduce the activity of the product. Glucose, 58 gm., and glucose, 50 gm., plus lactic acid, 8 gm., manifest exactly the same increases above the basal metabolism, 4.7 and 4.6 calories, respectively. Lactic acid therefore behaves like an intermediary metabolite of glucose and not like alanin which would have shown a summation effect. Glucose, 50 gm., plus acetic acid, 3 gm., shows an increase of 7.23 calories per hour. This indicates a summation of the influences of the two factors involved; it is identical with the behavior of glucose and fat when given together and in the author's opinion it supports the conception that acetic acid is an intermediary metabolism product of fatty acid by B-oxidation, and renders questionable the idea that acetic acid is an intermediary product of glucose metabolism.

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**Animal Calorimetry. XIX. The Influence of Acids upon the Carbon Dioxid Combining Power of the Blood Plasma.**

*Sophia A. Taistra, J. Biol. Chem., 49:479, Dec., 1921.*

This paper deals with the reduction in the quantity of sodium bicarbonate in the blood after administering acid substances to a dog in quantities which are comparable with the amounts given to the same animal in the calorimeter experiments described in the preceding paper by Lusk. It is known that the reduction in alkali reserve of the blood plasma does not change the actual hydrogen-ion concentration of the medium. The method used was to determine the change in the carbon dioxid-combining power of the plasma with the apparatus of Van Slyke. The different substances were always given in a broth containing Liebig's extract of beef. The author's tabulated results show that glucose, 50 gm., and acetic acid, 3 gm., which cause the greatest increases in meta-

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bolism have no effect whatever upon the carbon dioxid-combining power of the blood, whereas glycocollic acid, lactic acid, and hydrochloric acid, which have comparatively little influence upon the heat production, produce a profound depression of the carbon dioxid-combining power. The specific dynamic influence of the foodstuffs is therefore not attributable to the introduction of acid metabolites in the blood stream.

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**Animal Calorimetry. XX. The Influence of the Ingestion of Meat and Glycerin and Alanin upon the Carbon Dioxid Combining Power of Blood Plasma.**

*Alfred Chanutin, J. Biol. Chem., 49:485, Dec., 1921.*

The author states the problem discussed in this paper as follows: Do the amino-acids formed after the ingestion of meat by a dog so reduce the alkali reserve of the blood that this becomes a contributing cause of the great increase in heat production known as the specific dynamic action of meat? In the author's experiments the amino-acids were administered in a warm broth to a dog, the broth containing 2.5 gm. of Liebig's extract and 500 c.c. of water. The tabulated results show that there is always an increase in the carbon dioxid combining power of the blood following the ingestion of meat, of glycin, or of alanin. The broth itself was found to be without influence. Since the administration of bicarbonate of sodium has no influence upon the heat production of a dog, it is evident that the great increase in the heat production which takes place during the hours immediately after the ingestion of meat is not determined by any change in the alkaline reserve of the blood, nor can such change be interpreted as being even a participating element in the causation of the phenomenon, the author believes.

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**Some Nutritive Properties of Nuts. II. The Pecan Nut as a Source of Adequate Protein.**

*F. A. Cajori, J. Biol. Chem., 49:389, Dec., 1921.*

The author has previously observed that young rats would grow at a normal rate and attain adult size on diets in which the essential source of the protein of the ration was derived from various nuts. With the exception of the pecan nut, successful feeding trials resulted with all the nuts investigated. The rations containing the pecan nut as the source of protein were complete in every other known dietary essential. The failure of rats to grow at a normal rate on such diets may be due, the author believes to either one of the following causes: (1) the proteins of this nut may yield insufficient amounts of those amino-acids that determine the nutritive value of a protein; or (2) the pecan nuts may contain some substance which renders rations of which it is an important component distasteful or injurious to rats. The author studied the proteins of the pecan nut, the Van Slyke method being used for protein analysis. The investigation revealed that pecan meal contains, as its principal protein, a globulin, salted out by 0.5 saturation with ammonium sulphate and coagulated at 79°-86° C. There is evidence of a trace of an albumin, which starts to coagulate at 55°-60° C., and is precipitated by ammonium sulphate only at a point of complete saturation. The author then undertook the preparation of a pecan globulin. He found it to be a light gray powder, with no evidence of crystalline structure,

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containing 15.76% nitrogen and 0.83% sulphur, calculated on a moisture-free and ash-free basis. The distribution of the nitrogen in this globulin as determined by the Van Slyke method, after complete hydrolysis with 20% hydrochloric acid, was investigated by the author and the results tabulated in the article. Since the globulin yields large amounts of basic amino-acids, it seems highly improbable that the failure of rats to grow, when the pecan nut furnishes the protein of their ration, can be attributed to an amino-acid deficiency.

The shelled pecan is bitter and astringent because there is a large quantity of tannin in the outside cuticle. The astringency that this amount of tannin gives to diets made up in large parts of pecan nuts or pecan press-cake, the author shows, renders such rations unsuitable for rats. In the first of 2 series of experiments on rats the pecan nut was incorporated in the diet in the form of a press-cake after the tannin had been removed from the surface of the nut by treatment with hot sodium hydroxid. The animals grew at a normal rate. In the second experiment of the series, the diets contained pecan nuts from which the tannins had not been removed. The results show a failure of normal growth of rats in the second experiment, indicating, the author says, the effect that some distasteful or injurious substance in the food may have on the growth of rats.

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On the Mode of Functional Changes in the Glandular Structure.

R. Tsukaguchi and K. Takagi, *Japan Med. World*, 1:7, Tokio, Nov. 15, 1921.

This study is concerned with the changes in the cellular body of the gland, not with those of the nucleus. The old idea that the secretory function of a gland is represented by changes in the granules, is borne out. The granules appear to a marked extent in resting stages of the cells, and when secretion begins they gradually decrease and finally disappear; they are changed into secretion. According to the stage of functional activity, the glandular cells diminish in size and become dark, or they may increase in size and become clear. Illustrations of the cells of a dog's pancreas during the staining process show zymogen granules just being formed to secretion. As a special feature of each granule, there is a transparent ring directly around it. This feature is more distinct in certain cells, while the granules in the center of the ring become smaller and lose their characteristic staining ability, remaining only as faint bodies, a part of them disappearing entirely. The final picture represents the granules as clear vacuoles of about the same size as are seen in the cell. During this process the plastosome—the constituent which has direct concern with glandular activity—remains in the base of the cell; some may be seen between the granules and vacuoles, but there are no morphological changes. Of the various theories as to what place the plastosomes (or mitochondria) take in the function of glandular cells, the view here favored is that they have direct relation with the origin of the secretory granules, in fact, that they are the mother material of these granules. According to these observations, the ring around the granules, known as hyaloplasm, appears only at a certain functional period; therefore, it must be a transitory structure, though other investigators have believed it to be a con-

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stant structural element of the cell. The most rational view as to the nature of the vacuole, the authors think, is that it is a secretion matter elaborated by the granular changes and kept in the cell just before being secreted. The mode of granular changes is different in each kind of gland and sometimes requires diverse explanations in the same gland. The thyroid was also studied here. Several tissue cells of the mucous membrane of the uterus, placental tissue, and carcinoma of the uterus present structures very much like the epithelium of the thyroid or the pancreas. Though each has its own type and degree of glandular structure, it presents, structurally, the same changes. Therefore, the physiological or pathological modes of function in all of these structures may be said to be a mode of secretion resembling glandular function from the purely morphologic point of view.

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**Effect of the Hypophysis on Growth.**

*B. Houssay and E. Hug, Compt. rend. Soc. de biol., 85:1215, Paris, Dec. 17, 1921.*

Twelve series of experiments in dogs, since 1908, are available for report. Most animals soon recovered from the operative removal of the hypophysis and appeared normal for a certain time. Aside from variable postoperative symptoms, the principal result was retarded growth, apparent in one to two and-half months. Growth may cease entirely or partially. A few dogs continued to be normal, but remains, or small portions of the intermediate portion of the hypophysis were found at autopsy in such cases. In some cases where growth was arrested, one-fifth to one-third of the gland was found still present at autopsy. Either the gland is not invariably essential for growth, or the symptoms are due to lesion of the infundibulum. The animals often become remarkably fat. The temperature usually remains normal; in a few cases, it was subnormal. No temperature rise was obtained by injecting decoctions of the anterior lobe. Hypophyseal grafts in the thyroid degenerated without producing any effect. Improvement could not be obtained by feeding the entire bovine hypophysis or its anterior portion; on the contrary, the effects were sometimes unfavorable. Intra-peritoneal injections of fresh gland were also negative. The modifications induced by removal of the hypophysis include changes in character, alterations in the genitals, thyroid and thymus, besides the growth retardation and obesity. It cannot yet be stated whether the symptoms are of glandular, or nervous, origin.

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**Physiology of Glands. XLVIII. Respiratory Metabolism in the Splenectomized Dog.**

*Chu Koda, Biochem. Ztschr., 122:154, Berlin, Sept. 26, 1921.*

The removal of the spleen in the rat produced a rise in the respiratory metabolism. From this it was concluded that the thyroid gland and the spleen act antagonistically in regard to respiratory metabolism, because thyroidectomy reduces the respiratory exchange (elimination of CO<sub>2</sub> and water). Experiments on dogs were accordingly performed. First, the fundamental exchange of gases in the normal animal during a period of ordinary feeding was ascertained. In a second experiment, carried out in the respiration chamber, 30 gr. of peptone in 200 c.c. of

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water were given in order to induce increased hepatic activity. The weaning of the animal was then undertaken and the respiratory metabolism under ordinary feeding and after ingestion of peptone was studied in a series of experiments.

The results showed that splenectomy in the dog does not exercise any observable effect on the exchange of gases. Hence, the conditions differ here from those obtaining in the rat.

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**Physiology of Glands. XLIX. Respiratory Exchange in Splenectomized Dogs and Dogs Fed on Iron-Free Foods.**

*Francis H. Doubler, Biochem. Ztschr., 122:161, Berlin, Sept. 26, 1921.*

The spleen retards respiratory metabolism whereas the thyroid gland promotes it. But the spleen also plays a part in the metabolism of iron. In normal and in splenectomized rabbits, the red blood corpuscles are regenerated equally well so long as the food contains the requisite amount of iron. As soon as iron is eliminated from the food, the diminished capacity of the splenectomized rabbit for blood regeneration is observed.

The researches were carried out in a Jaquet's metabolism apparatus, the gas analysis in a Haldane's apparatus. The respiratory exchange of gases under a normal diet was studied. Upon this followed a period of iron-free feeding and then splenectomy was performed. Finally, there followed a sustained period of iron-free feeding. The tabulated figures show that the combination of 2 interferences, viz., removal of the spleen and withdrawal of iron from the food, do not demand any variation in the respiratory exchange in the dog for the length of time occupied by the experiments. Further, splenectomy and elimination of iron do not affect, in any way, the coagulation-time of the blood. The amount of hemoglobin in the blood is obviously very resistant toward these interferences and is only reduced slowly.

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**Intestinal Movements and Irritability of the Splanchnic Nerve after Ablation of the Adrenals.**

*E. Wertheimer and E. Duvalier, Compt. rend. Soc. de biol., 85:997, Paris, Nov. 26, 1921.*

The splanchnic nerve responds to stimulation independently of adrenalin. With the object of ascertaining the extent of this independent irritability, experiments were made on dogs and cats. Five hours after removal of the adrenals, the chloralosed animals were subjected to splanchnic irritation, which induced relaxation of the intestine and arrest of its movements; these results were also obtained seven hours after ablation. When arterial pressure is low (2 to 3 cm. of Hg), the excitability of inhibiting fibers sometimes survives that of the vasomotors, the intestine relaxing during stimulation, without increase of pressure. Probably by exciting the peripheral endings of the splanchnic, adrenalin may arrest intestinal movement; if a small dose of adrenalin (5 c.c. of a solution of 0.002 mg. per c.c.) be injected into the saphenous vein, prolonged intestinal inhibition results without concomitant elevation of pressure, or with increase of only 1 or 2 mm. Hg. The intestine does not share the asthenia induced in skeletal muscles by removal of the adrenals;

intestinal movements maintain their original vigor and are even reinforced at the moment of cardiac arrest and immediately after death. These findings are contrary to those of De Mira and Fontes, obtained in rabbits, the different conclusion being doubtless due to the different animals studied.

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**Technic of the Extirpation of the Medullary Portion of the Suprarenal Capsules.**

*B. Houssay and J. Lewis, Compt. rend. Soc. de biol., 85:1209, Paris, Dec. 17, 1921.*

This method permits preservation of the cortex. Ether anesthesia is necessary. The dog lies on the right side. The incision, beginning 5 cm. above the last rib, descends below the costal border and then turns outward. It is from 17 to 25 cm. long. The skin is covered with compresses. The thick aponeurosis covering the lumbovertebral muscles is incised longitudinally, as high up as possible. It is then turned outward and the abdominal wall carefully sectioned. A lumbar fasciculus of vessels and nerves should be ligated from behind forward. The work should be carried as high as possible without opening the pleura. It is necessary to go up to the last intercostal vessels, under the last rib. Loose connective tissue is separated with the hands, and the kidney is turned obliquely inward and downward. A retractor is introduced above, its face against the costal border. From this moment the operator must wear a frontal lamp. The operative field is widened by turning the kidney downward and outward. The left suprarenal comes into view. The lumbocapsular vein is liberated on the external surface and border of the capsule, up to the point where it adheres strongly at the beginning of the internal surface. The lower pole of the capsule is freed with a cannulated sound to nearly one-fifth of its extent, adhesions or vessels being cut. The upper pole is freed by cutting the branches of the splanchnic nerve and tearing through the vessels. If the freeing is well done, the capsule will retain important vascular connections and be movable. The lumbocapsular vein is then drawn above the upper pole. A long, curved clamp is applied, tight enough to prevent slipping but not enough to injure the pedicle. By elevating the clamp, the capsule presents by its external border. With one edge of a razor blade the capsule is split longitudinally along the external border. Its longitudinal axis must be kept straight; this can be done with a forceps having wide and flat teeth, or by the thumb and index finger. Being split, the capsule is opened like a book. With the aid of the clamp, it is easy to scrape out the medullary substance with a curette. The borders may be held by a forceps. When the medullary portion is removed, and the curette scrapes against the cortex, the 2 halves of the capsule may be sutured with fine catgut, and the forceps is removed. Hemorrhage is of no moment. The wall is sutured in 2 planes. The following are the important points: Very high incision; frontal illumination; careful, but not excessive, freeing of the upper and lower poles; a clamp to lift and steady the capsule; a short razor blade; complete curettage of the medulla, with little injury of the cortex. The operation is much easier in the living than in the dead animal, because the dead organ rapidly softens.

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**Comparative Importance of the Medullary and Cortical Portions of the Suprarenal Capsules.**

*B. Houssay and J. Lewis, Compt. rend. Soc. de biol., 85:1210, Paris Dec. 17, 1921.*

The authors experimented with 16 dogs. Total extirpation of the suprarenals produced death in forty-eight hours. Almost total extirpation was also fatal, with typical symptoms. In 3 dogs dying within forty-eight hours, the cortical lesions were probably too great, removal of the medulla alone having been attempted. All the animals of which only the medullary portion of the capsule was removed, with the exception of the 3 mentioned above, survived, appearing normal. Their functional conditions will be reported later.

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**Pancreatic Diabetes in Dogs Deprived of the Medullary Portion of the Suprarenal Capsules.**

*B. Houssay and J. Lewis, Compt. rend. Soc. de biol., 85:1212, Paris, Dec. 17, 1921.*

The medullary substance of the left suprarenal, and the entire right suprarenal, were removed from 5 dogs. About a month later, when the dogs had recovered, the pancreas was extirpated. The resulting alteration in glycemia and glycosuria was then studied. Of the 5 animals operated on, 2 survived (eight and three days, respectively). Hyperglycemia varied from 0.7 per 1,000 to 4 per 1,000, in one animal, and from 0.8 per 1,000 to 3.63 per 1,000, in the other. The urinary glucose rose to 10%. The medulla was entirely removed in the animal surviving 8 days and presenting the highest glycemia and glycosuria. A very minute fragment remained in the other. Of the other 3 dogs operated on, 1 died of peritonitis four days after removal of the pancreas, the other 2 in six and twenty-four hours, respectively. The results are conclusive only for 1 of the experiments. Further studies are in progress.

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**Karyorrhexis in the Human Thymus.**

*A. Dustin, Compt. rend. Soc. de biol., 85:1103, Paris, Dec. 10, 1921.*

In young, fasting animals, the thymic cells disappear by condensation and degeneration of the nucleus (pyknosis), followed by phagocytosis accomplished by large macrophages. The cells are destroyed in man not only by pyknosis, which is physiologic and benign, but by degeneration and rupture of the nucleus (karyorrhexis). The latter process was observed in adults, as follows: To a limited degree in cases dying within a few hours from extensive trauma; abundantly in acute gaseous gangrene and wound infection; and to a greater or less extent in other infections. In children, karyorrhexis was observed, also in infectious processes (bronchopneumonia, tuberculous meningitis and endocarditis affecting the mitral valve).

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**Bovine Thyroidectomy.**

*E. Hug, Rev. Asoc. médica argentina, 34:731, Buenos Aires, Sept., 1921.*

Three animals were thyroidectomized at about two months of age, and their growth compared with a normal control. Two males and one  
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female were studied. No disturbances of importance were noted except that the growth curve was rather lower than in normal animals. They continued to be undersized but the ordinary secondary sexual characteristics developed. No symptoms of hypothyroidism were noted. The blood picture was normal. These results are in contrast to other experiments on animals which show marked disturbances after thyroidectomy.

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**Thyroidectomy in Calves.**

*E. Hug. Compt. rend. Soc. de biol., 85:953, Paris, Nov. 17, 1921.*

The gland was extirpated in two calves aged 2 months and in one aged 3 months, and the animals were observed for nineteen months following the operation. Retarded growth was the only general symptom; physical condition was excellent and secondary sexual characters well developed. Calcium content of the blood was the same as in control animals.

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**Rôle of the Nucleus in Epididymal Secretion.**

*J. Benoit, Compt. rend. Soc. de biol., 85:946, Paris, Nov. 17, 1921.*

Not only chondriome and cytoplasm, but also the nucleus, are concerned in secretion. Epididymal epithelium of man and of the bull, horse, dog, etc., has been examined. The secretory product occurs in two forms; the cell may be crowded with acidophilic granules, or, in its basal portion, may contain a single, large, acidophilic mass. In the first secretory stage, intracytoplasmic granules are few. The nucleus becomes gradually crowded with granules, the nuclear membrane becomes distended, finally ruptures, and the granules escape into the cytoplasm, where they form large masses. This process is identical in horse, dog and man. The process is sometimes varied by gradual escape of granules from the nucleus. In the bull, the apical portions of the cells bud into vesicles which project into the lumen of the epididymis, granules and nuclear matter being liberated. In the former and more easily demonstrated process, large granular masses escape from the cytoplasm into the lumen. It will be shown in later reports that the secretory products of the nucleus are accompanied by lipoids and substances of cytoplasmic origin. The combined cellular secretion nourishes the spermatozoa during their stay in the excretory passages of the testicle. The spermatozoa are there removed from other sources of nutrition, are largely composed of nuclear substances and the nuclear secretion is adapted to meet their special nutritive requirements.

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**Mineral Substances in the Animal Economy. Action of Karlsbad Water on the Anions in the Rabbit.**

*Emil Stransky, Biochem. Ztschr., 122:1, Berlin, Sept. 26, 1921.*

These researches sought to determine whether sulphates could partially replace chlorids in the organism. Sulphates occur in many mineral waters in large quantities and besides exerting a local purgative action, they may possibly participate in the resorptive effects attributed to these waters. The behavior of chlorids, phosphates and sulphates administered in the form of Karlsbad water and in a mixture of potassium and sodium sulphates in the proportion found in Ringer's solution was studied.

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The experiments were conducted with rabbits fed on oats. For eight days the animals were left to become accustomed to the metabolism cage, being given oats and faucet water. Then in two principal periods of eight and five days each, the drinking water was replaced by Karlsbad water, or by the artificial water mentioned in the foregoing. Then followed secondary periods of five and eight days each on ordinary water. Urine and feces were measured daily, and the amounts of water and oats ingested, as well as the body weight, were noted continuously. Chlorids and sulphates in the drinking water, and sulphates in the artificial water, were determined analytically. For Karlsbad water, the figures given by Ludwig were used. In oats and feces, the chlorids, sulphates and phosphates were estimated after destruction of organic matter and the performed anions estimated by extraction with nitric acid. The general condition of the animals was observed by determination of the nitrogen equilibrium. Chlorids in urine and feces were estimated by the method of Moraczewski, and phosphates by the Neumann Woy method.

The results of the two experimental series (Karlsbad water and artificial water) were as follows: The sulphates in Karlsbad water are completely absorbed. During the period of administration, they are partially retained and exert no influence on the exchange of chlorids in the organism. On the other hand they exert a powerful influence on the phosphates that are retained in the organism, and in this process anions are formed, though not in as large amount as cations. The same effect is produced by physiological mixture or sulphates, so that the effects induced by the administration of Karlsbad water in animals may be looked upon not merely as the action of the specific cation mixture, but likewise as resulting from the preponderance of sulphate ions. In general, better assimilation of the food occurs, manifested by an increase in the total nitrogen equilibrium.

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### 1b. BIOLOGIC AND ORGANIC CHEMISTRY

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#### A Buffered Physiologic Salt Solution.

*Alice C. Evans, J. Infect. Dis., 30:95, Jan., 1922.*

Evans describes a simple method for the control of the H-ion concentration of physiologic salt solution. The controlling agent is a phosphate mixture prepared according to Sørenson. The procedure is as follows: A m/15 solution of primary phosphate is prepared by adding 9.078 gm.  $\text{KH}_2\text{PO}_4$  to 1 liter of distilled water. A m/15 solution of secondary phosphate is prepared by adding 11.876 gm.  $\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$  to 1 liter distilled water. A mixture of 6 c.c. of the secondary solution and 4 c.c. of the primary solution has a pH value very near 7. A mixture of 8 c.c. of the secondary solution and 2 c.c. of the primary solution has a pH value very near 7.4. A solution of any other desired concentration can be obtained by altering the proportions of primary and secondary solutions. For the preparation of the isotonic buffered salt solution 1 part of phosphate mixture of the desired H-ion concentration is added to 9 parts of 0.9% NaCl solution.

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**A Simple Rapid Method of Determining Surface Tension in Small Quantities of Fluid.**

*R. Brinkmann and E. Van Dam, Münch. med. Wochenschr., 68:1550, Dec. 2, 1921. Also Nederl. Tijdschr. v. Geneesk., 65:2905, Haarlem, Dec. 10, 1921.*

The authors use the torsion balance of Hartmann and Braun, with which it is possible to measure the force required to break the surface film adhering to a ring as it is drawn out of a fluid. A platinum ring is fastened with a loop of platinum wire to the torsion balance. The determination is simple. The balance is so arranged that it is in equilibrium. The indicator shows the weight of the ring and platinum loop. The solution to be examined is placed in a watch crystal under the ring. The balance is fastened and the watch crystal is carefully raised by means of a screw stand until the surface of the fluid just touches the lower side of the ring. The balance is then freed and the force that suffices to lift the ring away from the fluid is determined. This force is designated "K." It can be measured within less than 0.5 mg. Next the watch crystal is lowered and the ring and adherent fluid is weighed. This factor is called "G." The surface tension is then K minus G, divided by L (the latter being constant for any given ring). L is determined by using a pure fluid with a known surface tension, such as pure water at a given temperature. The weight of the watch crystal and platinum ring must be subtracted from the measurements. The method has the advantages of accuracy, simplicity, rapidity and direct reading, and is also suitable for colloidal solutions.

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**Precipitation with Lead.**

*Hedwig Langecker, Biochem. Ztschr., 122:34, Berlin, Sept. 26, 1921.*

Lead acetate finds general application in biologic chemistry for purification and precipitation; varying proportions of lead oxide and lead acetate may be advantageously employed. Solutions of lead acetate were prepared by mixing definite quantities of both substances (air-dried) and treating the mixture with hot water. Concentration, alkalinity and lead were then determined in each case. A table shows that the 1/2, 1, 2, and 3 basic lead acetate were obtained in solution. The 1/2 and 1 basic lead acetate were dissolved entirely, whereas the others left a part undissolved. Therefore, highly concentrated solutions can only be obtained in the case of low basicity exponents. For preparing the solutions equivalent quantities of air-dried lead oxide and lead acetate should be triturated until a nearly white mass is produced, a little hot water added with stirring and the mixture brought up to the required volume and filtered. Precipitation with lead acetate solutions increases in efficacy in the order acid, basic, neutral solutions, up to solutions possessing increasing basicity exponents.

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**Experiments on the Possibility of Electrolysis of Cells, Component Parts of Cells and Membranes.**

*Karl Heesch, Pflüger's Arch. f. d. ges. Physiol., 190:198, Berlin, Oct. 4, 1921.*

Comparison was made with red blood-cells and other cells, such as spores of lycopodium and leukocytes, to determine the degree of possible electrolysis. Cell substances such as India rubber, agar, cellulose, starch, cholesterol, lecithin, oil and albumin were examined by the cataphoresis apparatus of Höber. The electrolytic capacity was also determined by electroosmosis by employing the substances in the form of membranes. Collander's results were the starting point of these researches. Collander worked on the plasmolysis of plant cells and von Linzenmeier worked on the electrolysis of negatively charged human red cells after treatment with m/500 to m/1,000 lanthanum salt. Except for India rubber and agar, the negatively charged cell constituents suspended in sugar and salt solutions were electrolyzed by lanthanum ions in concentrations of m/100 to m/500. Yeast and lycopodium cells showed the same reaction probably as a result of the condition of the coat or enveloping substance of the cell. The celluloses were impregnated with lipoids, soaps, etc. The red and white blood cells do not react in this way. They are electrolyzed for some unknown reason only after thorough washing with salt solution and treatment with m/10 lanthanum. Histon and clupein sulphate have an electrolytic action but the salts of alkaloids do not.

The electrolytic effect may be increased or decreased (positive and negative sensitization) by previous washing in a cane sugar and salt solution in which other substances are dissolved. Albumin and gelatin have a positive effect while the effect of India rubber and agar is negative. Lecithin is better than cholesterol. The importance of the composition of the cell medium in relation to the electric charge of the cells may now be appreciated. The organic colloids on the surface of the cells are the decisive substances. It is possible that these studies will solve the question of agglutination, cytolysis and similar phenomena.

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**The Composition of Chinese Edible Birds' Nests and the Nature of Their Proteins.**

*Chi Che Wang, J. Biol. Chem., 49:429, Dec., 1921.*

The edible birds' nests are gelatinous substances produced by certain swifts, the *Collocalia*, natives of Malaya and Ceylon. The source from which the birds make the nests has been uncertain. Certain observers have thought the source a secretion from the swifts themselves, and one observer found in the birds 2 large salivary glands which secreted much viscous mucus. The observations given in this paper show that the nests consist largely of a mucin-like substance and, therefore, are in accord with the secretion theory. This author studied the general properties, the chemical composition, the artificial digestion, the carbohydrate radicle, and the biological value of the proteins. The tabulated results show that the Chinese edible birds' nest has the properties of a protein as well as those of a carbohydrate. It belongs, therefore, to the class of glycoprotein. Its percentage composition resembles that of salivary mucin. Its ash is high, but there is no

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sandy material present. It contains 10.29% nitrogen and at least 17.36% carbohydrate. The author's artificial digestion experiments indicated that the birds' nest was digested by both pepsin hydrochloric acid and trypsin at a slower speed than boiled egg. The distribution of nitrogen showed a higher value for both humin nitrogen and cystin nitrogen than for pure proteins. The former is probably due to the carbohydrate radicle in the nest while the latter is due to the presence of fine feathers. Other fractions were similar to those of pure proteins. Feeding experiments indicated that the nest protein is probably of an inferior quality. It failed to supplement a ration adequate in all respects, except that the source of the protein was derived from either maize kernel or rolled oats.

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**The Isolation and the Nature of the Amino Sugar of Chinese Edible Birds' Nests.**

*Chi Che Wang, J. Biol. Chem., 49:441, Dec., 1921.*

The author's technic for the isolation of the carbohydrate of the nest is as follows: About 300 gm. of the birds' nest were heated with 2,100 c.c. of 3% hydrochloric acid for five hours until the material had completely gone into solution, but no black precipitate was produced. The hydrolysis solution was evaporated to dryness over sulphuric acid and under solid sodium hydroxid in vacuum desiccators at room temperature. The thick black residue was extracted with 95% alcohol and the alcoholic solution was separated by centrifuge. The extraction was continued until the alcoholic solution gave a little or no reducing power. It required from fifteen to twenty extractions, at least. The alcoholic solution was evaporated to a very thick, dark-brown syrup under diminished pressure (30 mm.). The syrup was then taken up with about 500 c.c. of methyl alcohol. A fairly large quantity of brownish crystals thus resulted. They were filtered off and redissolved in a little boiling water. The solution was filtered again and the brownish filtrate was treated with about eight times its volume of absolute alcohol and then with ether until no more precipitate formed. The crystallization was repeated until the crystals became pure white and seemed to be uniform on microscopic appearance; rods grouping themselves in the forms of an elaborate fern leaf. The yield was about 10 gm. As the properties of this product seemed to be more or less different from those of any of the known amino sugars, it was thought possible that the product might be a mixture instead of being a single compound. Another preparation was therefore made by the author according to the method given above, except that in dissolving the brown crystals from methyl alcohol, less water was used and instead of using both absolute alcohol and ether to bring about the precipitation, only the former was used. This required at least 1,500 c.c. of absolute alcohol. The alcoholic solution yielded a large crop of about 5 gm. of beautiful precipitate on standing over night. It was filtered by suction and after being recrystallized twice, was dried over sulphuric acid. There were various forms of crystals in this fraction but the "Kreissector" form of Muller predominated. The alcoholic filtrate was treated with ether until the solution became cloudy. On standing over night another crop of about 5 gm. of pure white crystals was obtained. It was filtered and dried as before. The

crystals of this fraction were large fluffy flakes. The three sets of crystals were found by the author to be very soluble in water and 80% alcohol, fairly soluble in 95% and in methyl alcohol, slightly soluble in absolute alcohol, and insoluble in ether, chloroform and acetone. All of them had a sweet taste and gave a strong test with both Molisch's and Fehling's reagents. They failed to respond to any of the protein reactions. When boiled with strong sodium hydroxid they gave off ammonia. None of them melted when placed side by side in melting point tubes and heated to 250° C. in a glycerol bath. The author gives in considerable detail the percentage composition of the alcohol-ether crystals; of the alcohol fraction; and of the ether fraction. He states that an examination of the properties and the analytical data of the three sets shows that they are all hexosamin hydrochlorides and that they differ from each other only in their optical rotation and the temperature at which they begin to turn dark on heating.

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**Chemical Constitution of Protoplasm.**

*Heinrich Walter, Biochem. Ztschr., 122:86, Berlin, Sept. 26, 1921.*

Complete analysis of protoplasm of higher plants presents difficulties, as many non-essential constituents must be eliminated. The plasma of higher plants behaves peculiarly under artificial digestion with pepsin, 0.5% HCl and tryptophan in 0.5% Na<sub>2</sub> CO<sub>3</sub>, inasmuch as it is not attacked unless previously extracted. After extraction with alcohol, ether and chloroform, pepsin digestion is incomplete, whereas treatment with trypsin effects rapid and complete solution. Spirogyra and yeast, on the other hand, behave quite differently. The plasma of the myxomycetes appears to behave like that of higher plants.

Plasma consists of an albumin component (plastin), which is capable of digestion by trypsin and is apparently related to the phosphoproteins, and a lipoid component, which interferes with the function of the digestive enzymes. It may perhaps be assumed that there is a chemical combination between the albuminoids and lipoids, which view is supported by Lepeschkin. Mere saturation with lipoids does not prevent the activity of the digestive enzymes, as may be demonstrated by soaking a piece of fibrin in solutions of rape oil, lecithin and chloroform and digesting it with trypsin at 40°. Probably, the lipoids are present in the entire plasma in a finely divided state and become visible only when disintegration has taken place. This explanation is in agreement with the conception that the plasma is an emulsion colloid. As plasma without colloids does not exist, the colloids must be considered a part of the plasma constituents. With the exception of the foregoing bodies poor in nitrogen (12% N), those containing phosphorus (2.15%) and sulphur (0.33%), no simple albuminoids occur in plasma, or they are to be looked upon merely as reserve substances.

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**Peculiarities in the Chemical Composition of the Brain in Infants.**

*Er. Schiff and E. Stransky, Jahrb. f. Kinderhik., 96:245, Berlin, Nov. 21, 1921.*

The functional peculiarities of the nervous system of the infant, are either in a general way due to the morphologic structure, or they

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appear only as dependent on certain constitutional factors. Here belongs in the first place the predisposition to convulsions, which is present only in some infants, and which disappears as they advance in years. The increase of volume of the brain in rickets, which is not due to an increase in tissues, must probably be considered as a swelling-out process. Through abnormal condition of the brain colloids, an increase of volume of the brain results which is not caused by hyeremia, nor by exudation or transudation, nor by tissue changes. Symptoms of edema of the brain, which appears mostly in acute infections, intoxications or brain diseases, are pressure on the brain, disturbances of consciousness, epileptic and catatonic manifestations. Such symptoms appear only in suddenly developed edema of the brain, and are perhaps the cause of convulsions in rachitic children; the slow development may be without symptoms through compensatory arrangements. Even under physiological conditions, the larger amount of water in the infant organism demands an increased swelling of the brain in infants. The authors made chemical examinations of the infant brain with the assumption that the swelling is influenced by the chemical building up of the colloid substances. It was presumed that the differentiation of the embryogenic brain, the separation into gray and white matter, the marrow formation and so forth, goes hand in hand with chemical changes of the brain substances. Because of the great importance of lipoids in the composition of the brain, particular attention had to be given to these bodies. Little more is known about the chemical structure of lipid bodies except that they dissolve in certain organic substances in contrast with albuminous bodies, and that a separation of certain groups of lipoids is possible by fractional extractions with several solvents. The result of examinations on twelve brains was that the water content of the brain diminishes with increasing age; in a 7 month fetus, it is 91%, in adults 77%, while there is an increase of lipoids, in the fetus 32%, in adults 59%. In adults, the lipoids are 2/3 of the dried residue, only 1/3 is albuminous substance; in young infants the lipoids are only 1/3 and they increase gradually. The acetone fraction (cholesterin) is remarkably high in infants, on an average 23.5% of the dried residue, twice as high as in adults. The aether petrolei fraction (unsaturated phosphates) is very low in infants, 9% of the dried residue compared to 28% in adults. The benzol fraction shows a similar action, 2% : 13.5%. The alcohol fraction (saturated phosphates) 3.8% : 6%. The amount of nitrogen, with the exception of 2 cases of rickets, showed a gradual decrease with the progressive development. The brain of infants is therefore richer in albuminous, and poorer in lipid bodies than that of adults, more than half the brain lipoids consist of bodies soluble in acetone, probably caused by the incomplete differentiation of the gray and white matter. The cortex is poor, the white matter rich in cholesterin; with advancing age the latter decreases, and in its place appear unsaturated phosphates and other lipoids. All mentioned peculiarities of the infant brain favor the development of swelling and explain the predisposition of convulsions, supposing that this hypothetical connection is correct.

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**Sulphate and Esterified Sulphuric Acid in Normal and Pathologic Body Fluids.**

*W. Heubner and R. Meyer, Biochem. Ztschr., 122:120, Berlin, Sept. 26, 1921.*

Following researches on the effects of parenteral administration of sulphur in articular disease, body fluids taken from various patients were examined for sulphate and esterified sulphuric acid. Free  $H_2SO_4$  as well as  $H_2SO_4$  split by hydrolysis, and esterified sulphuric acid, were determined in the blood, articular punctate, mucin, coagulum and filtrate in patients suffering from diseases of the joints, who had undergone treatment with sulphur. In normal human blood serum over 0.02% sulphate ion was found, but after removal of albumin, it appears to be completely absorbed by the coagulum. In inflammatory exudates from serous cavities only two-thirds as much sulphate ion as occurs in serum was found, besides lesser amounts of esterified sulphuric acid. With parenteral sulphur injections in articular affections esterified sulphuric acid in the blood serum was increased during the stage of febrile reaction, so that it could be observed even after removal of albumin. In a case of articular effusion, more esterified sulphuric acid was found than in the exudates from serous cavities. Therefore, articular cartilage would seem to be the seat of an increased production of these sulphuric acid combinations and hence the therapeutic effects observed after the administration of sulphur appear to rest on a chemical basis.

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**Alcoholic Fermentation; Fermentable Substances and Experimental Variations (Concluded).**

*Ramón Pelayo Morales, Gac. méd. catalana, 59:245, 280, Barcelona, Oct. 31, Nov. 15, 1921.*

The topic is discussed under headings of: general ideas and modes of action, history and theories, and susceptible substances and their respective variations. Various classifications are presented (according to substrate, origin, morphology, etc.); chemically, ferment may be grouped as: (1) Hydrases (sucrase or invertin, assimilase or diastase, cellulase, glucosidase, pepsinase, trypsinase and steaptase or lipase). (2) Reductases (reducing ferment, thus far inadequately studied). (3) Oxydases (amorphous, oxydizing ferment such as laccase and tyrosinase). (4) Anhydrases (ferments antagonistic to hydrases and typified by the ferment combining glycocoll with benzoic acid to form hippuric acid). (5) Coagulases (including lab-ferment and fibrinase). Pasteur's theory has survived all attack, but living ferment are not directly essential; the process is enzymic or chemico-vitalistic. Facts requiring explanation are: the very small quantities in which ferment are effective; unalterability by the reaction; cessation of action when subjected to temperature of 80° C., the optimum for ordinary reagents; abolition of fermentation by destruction of microorganisms and their reproduction, as occurring in sterilization by heat and filtration.

Fermentation is essentially chemical. Certain conditions as to moisture and temperature are necessary. Enzymes are composed of the same 5 elements as those which occur in proteins, and also contain mineral substances. Fermentation produced by enzymes is not affected

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by chloroform, salicylic acid, thymol; or other substances which are toxic to protoplasm. Serotherapy is essentially chemical. Of the various organisms capable of producing alcoholic fermentation, yeast is the most important. Yeasts vary considerably. The apiculatus variety ferments dextrose only, saaz yeast ferments dextrose and maltose, pombe and logos yeasts ferment dextrin, and so on. Beer yeasts are high and low, the first acting at 18° to 25°, the second at 4° to 10°. Fresh, active and well conditioned yeast ferments rapidly, producing alcohol and glycerin, with secondary products like succinic acid, fusel oil, etc. Sugars may be fermentable directly or require previous preparation by splitting. Alcohol may be produced by fermenting substances other than sugars. The juices of grapes, figs, plums, currants and cherries are directly fermentable, as also honey and manna; addition of yeast is not necessary, as fermentation is produced by organisms present in the air. Beer-root, sugar-cane and milk contain sugars not directly fermentable into alcohol but capable of conversion into fermentable varieties. Flours of rye, wheat, barley, corn and especially potato constitute examples of substances which are not sugars, but which may be converted into sugars yielding alcohol by fermentation.

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**Enzymatic Synthesis of Fructose-Zymophosphate.**

*Hans von Euler and Folke Nordlund, Hoppe-Seyler's Ztschr. f. physiol. Chem., 116:229, Berlin, Oct. 22, 1921.*

The part played by phosphates in the enzymatic splitting of sugars is only slightly clear, e. g., the production of the diphosphoric acid ester of fructose, an important phase of sugar splitting in the animal body, may be a pathologic process. It has been demonstrated that the same enzyme preparation can cause synthesis and hydrolysis, the enzyme acting as catalyst. To determine the influence of acidity during the synthesis of zymophosphate, the range of acidity was tested for different sugars, (glucose, fructose, maltose and cane sugar) using both fresh and dried yeast. The test solution was made up of 20 gm. sugar, 0.3 gm. potassium phosphate (primary, secondary or mixtures) 110 gm. water, 1 c.c. toluol or 10 c.c. of a 2.5% phenol solution. To this was added 10 gm. finely pulverized dried yeast, or 30 gm. fresh yeast, pressed dry. From time to time 5 c.c. were removed from this mixture, added to 5 c.c. of a 2.5% solution NH<sub>3</sub>, filtered from the yeast, and the filtrate mixed with magnesia mixture. After settling for twelve hours, it was weighed as, Mg<sub>2</sub>P<sub>2</sub>O<sub>7</sub>. The rate of fermentation in fermentation flasks kept in thermostat at 30° was determined. In order to keep the acidity of the solution at the same pH value during the entire synthetic reaction, in the alkaline solutions (pH>7), the CO<sub>2</sub> resulting from fermentation was constantly neutralized by the drop-wise addition of concentrated alkali; in the acid solutions (ranging from pH=7 to pH=5), the CO<sub>2</sub> was kept saturated by the addition of sodium bicarbonate with O<sub>2</sub>. In acid solutions (pH=5), such measures were not needed, since in such solutions the fermentation CO<sub>2</sub> does not alter the reaction of the solution. The electromotive measurements of acidity took place at an acidity of pH>7 under saturation with H, at pH=5 with simultaneous currents of H and O<sub>2</sub>. The acidity was further determined by the indicator method, using dibrom-o-cresolsulphonephthalein (cresol powder), cresol red and thymol blue as indicators.

Experiments on the effects upon coenzyme were also carried out. This coenzyme was made by digesting 5 gm. dry top yeast with 100 c.c. water at 80°, which sufficed completely to inactivate zymase while leaving the coenzyme intact. Furthermore, tests were made on the influence of phosphate concentrations, of toluol and phenol, on the effect of acidity on tests with glucose; the formation of zymophosphates with glucose and cane sugar; influence of the acidity in tests with fructose; comparisons between hexoses (fructose, glucose and galactose) and bioses (maltose and lactose). The results are summed up in a table, the length of time required under comparable conditions to combine one-half the phosphate present being determined by interpolation. An acidity optimum of pH=6.2-6.5 was obtained for the enzymatic zymophosphate production by bottom yeast. This is true for all sugars tested and agrees with the figures found by Euler and Heintze for total fermentation ( $\text{CO}_2$  production)—namely 4.5-7.0. The optimum action for saccharase lies more to the acid side, at pH=4 and at pH=7 its activity amounts to only one-third of the optimum; possibly an esterification of cane sugar occurs. The acidity curve of fructose appears to differ from that of glucose.

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**Estimation of Glucose in the Body Fluids.**

*G. Etienne and M. Verain, Compt, rend. Soc. de biol., 85:1080, Paris, Dec. 10, 1921.*

The authors have devised a colorimetric method, used in combination with curve-tracing. Chemically, the method depends on the principle that given quantities of glucose will decolorize Fehling's solution in a degree proportional to the glucose present. The glucose is estimated by comparing the thickness of a standard layer with that of the thickness required to make the color present after reduction correspond with that of the unreduced solution. Process: Prepare 2 samples of Fehling's solution (Pasteur formula) so that 4 c.c. will be completely reduced by 10 mg. glucose. To one of the samples add the liquid containing the glucose to be estimated. Boil for two minutes, cool quickly, make the volume up to 15 c.c. and centrifuge. The color obtained is compared with that of the unreduced sample, which is treated in the same way, except that no glucose is added. The colorimeter (Duboscq, small model) is checked by taking the average of 10 readings. The authors worked in a dark room, in order to insure retinal sensitiveness. For the curve tracing, the abscissa, running from 0 to 10 mg., is marked off in spaces corresponding to 0-5 mg. each. On the ordinate are marked the colorimeter readings in millimeters. The curve traced for the test is compared with standard curves traced for various thicknesses of the solution and the corresponding quantity of glucose is read from the abscissa. The curve reading is correct for thicknesses of 20, 25, and 30 mm. Layers of considerable thickness should be used because the color of thin layers cannot be accurately judged. The method is applicable to all body liquids after clarification. Patein's reagent is preferable for blood, urine and cerebro-spinal fluid, since it makes it possible to avoid error due to reduction by such substances as urea, uric acid or creatinin.

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**The Influence of Cations in Alkaline Glycolysis.**

*A. Slosse, Compt. rend. Soc. de biol., 85:1113, Paris, Dec. 10, 1921.*

If a solution of pure d-glucose is digested in the presence of an alkaline hydrate, fructose and d-mannose are produced. Alkaline carbonates, ammonia and sodium acetate produce the same effect as the hydrates. The author has made further investigation of the process. Glycolysis, maintained for an hour at a temperature of 60°, was studied by using decinormal and centinormal solutions of NaOH and KOH. Care was taken to eliminate microbic action. The intensity of the glycolysis was very different for Na as compared with K, notwithstanding the same content of OH ions. Variations in glycolytic action are therefore not due alone to OH ionic concentration. Na promotes glycolysis to a greater extent than K, or the effect of K is to retard glycolysis. This action of the metallic ion (cation) is not a biologic novelty.

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**The Approximate Lactose Molecular Constant.**

*M. Bouin, Compt. rend. Soc. de biol., 85:1089, Paris, Dec. 10, 1921.*

In natural milks, there is a reciprocal relation between the ash and the lactose, the former decreasing as the latter is increased. The author has expressed this relation by the constant 5 [weight of the lactose plus weight of the ash]. This constant has recently been criticised and is said to be less dependable than the constant [weight of the lactose plus 50]. The author finds that, for milks of the Montpellier region, the latter constant varies from 75 to 90, while the constant proposed by him varies only between 69.5 and 79.8. Expressed as per cent., the author's variation is 10.7, that of the other constant 13. The author's critic suggests substituting the factor 3 for the author's factor 5. To this proposal the author cannot agree, since the factor 3 represents merely an arbitrary selection and is neither more exact nor convenient than his original factor. In lowering the factor, the compensatory correction is diminished; the resulting figures will be too high for milks rich in lactose and too low for milks containing relatively little lactose. In expressing the general form of the constant as [weight of the lactose plus weight of the ash times K], the result most closely approximates the actual chemical findings when K is taken equivalent to 5.

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**The Influence of Hydrogen Ion Concentration on the Action of Pancreas Amylase.**

*J. Temminck Groll, Nederl. Tijdschr. v. Geneesk., 65:2541, Haarlem, Nov. 19, 1921.*

The literature of recent years relating to the influence of the concentration of hydrogen ions on fermentation gives little information regarding the amylases in spite of their importance. Only hyalin, the amylase of saliva, has been examined and it has been found that the optimum pH depends upon the anions present. Matheus has shown that the optimum action of the pancreas ferment takes place in an acid medium. This has been confirmed by the author's experiments, as shown graphically and in detail in tables.

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The Nature and Origin of Diastatic Ferments.

E. Rothlin, *Münch. med. Wchnschr.*, 68:1393, Oct. 28, 1921.

Biedermann has explained the fact that the activity of salivary ferment is increased by the presence of organic salts by the theory that the latter are considered as activators for the organic components, the zymogen, which are in themselves inactive. He has also assumed a regeneration of diastatic ferments—an amylose, without diastase, in the presence of inorganic salts. Experiments to ascertain whether the "autolysis" also occurs under aseptic experimental conditions showed a negative result, whereupon this process was attributed to bacterial infection and the view of Biedermann in regard to a regeneration of diastatic ferment from amylose in the presence of organic salts was rejected. Without having reconducted his tests under aseptic conditions, Biedermann has now rejected the theory of bacterial infection. But he has changed his original view, that a regeneration of diastatic ferment occurs from amylose in the presence of inorganic salts by autolysis, to one in which the autolysis is produced by traces of ferment remains in an inactive form (zymogen) which cling to the amylose and become activated by inorganic salts. Rothlin conducted experiments which led him to the conclusion that the views of Biedermann are not correct and that bacteria are the cause of the autolysis.

A 1% solution of starch kept for one hour at 80° C. was used as a substrate. This leads to the conclusion that the zymogen requires heat. By heating starch and starch solutions to 120° C. for one to three hours, no difference could be found in the autolysis experiment as opposed to ordinary solution of amylose. If the zymogen were stable to heat as a diastatic ferment, the autolysis with ordinary saliva (treated for one hour to 120°) ought to proceed much more rapidly because of the much greater ferment content, which according to the experimental results is not the case. Because of the tests on the effect of temperature upon the appearance of autolysis of amylose (Biedermann) it was expected that the tests under aseptic conditions would also be positive. To determine this the author sterilized a mixture of salt and amylose as well as salt and amylose solution separately, and subsequently mixed both solutions. There was no decomposition in both tests. These negative results almost conclusively proved that the autolysis depends upon a bacterial process. The proof was finally made conclusive by the fact that the expected autolysis actually occurred after a prolonged open contact with the air.

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Tannase.

Karal Freudenberg and Erich Vollbrecht, *Hoppe-Seyler's Ztschr. f. physiol. Chem.*, 116:277, Berlin, Oct. 22, 1921.

By means of tannase from aspergillus, the chlorogenic acid of coffee has been recognized as a depsid, a new sugar has been isolated from hainamelis-tannin, ellagic acid has been separated from the ester-like combination; hence it is of value to know about the activity of tannase preparations and systematically to increase the yield of tannase. By the action of equal amounts of enzyme upon 1,000 gm. tannin, 1,082 gm. of the methyl ester of gallic acid and 1,432 gm. digallol-glucose, the methyl ester of gallic acid can be used for the titration of (Sec. 1—Page 262)

tannase activity. For the titration 0.5% solutions are used, titrated with N/40 NaOH, litmus paper serving as an indicator. The optimum was put at 30°. The numerical expression for the activity of tannase preparations is their cleavage titer; this is the number of milligrams necessary to split 1,082 gm. anhydrous gallic acid methyl ester (1,000 gm. gallic acid dissolved in 200 c.c. of water) at 33° C. in twenty-four hours. It is important to regulate the hydrogen-ion concentration. Weakening of the acid which is formed leads to the splitting of the methyl ester. Tannase was prepared by boiling 600 gm. coarsely ground myrobalan in 3 liters water for ten minutes, extracting repeatedly. A solution of 9 gm. dipotassium phosphate is mixed with 3 gm. magnesium sulphate, the whole brought up to 12 liters, and tested with *Aspergillus niger*. After four days the growth is rubbed up into a thin pulp and left to itself. The acid produced is diluted, thus greatly increasing the yield of tannase. The expressed juice is cleared with infusorial earth. Upon addition of 5 times the volume of alcohol, tannase is precipitated in light flakes, and dried; it is neutral to litmus. If the light gray powder reduces Fehling's solution, it must be reprecipitated. It is capable of splitting cane sugar, cellobiose, maltose and inulin.

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#### Origin of Osmium-Reducing Fat in the Hepatic Cell of the White Mouse.

R. Noel, *Compt. rend. Soc. de biol.*, 85:1030, Paris, Dec. 3, 1921.

The origin of intracellular fat has been ascribed to the granules, chondriome and other structures. Iron hematoxylin was used to stain cells fixed by the methods of Regaud and Meves. The results indicated a relation between fat and chondriome and suggested that the fat might be elaborated by the mitochondria. Careful studies were made. The results are illustrated by a plate. The fat is elaborated by the chondriome, occurring at the surface of mitochondria or chondriocentes. Osmium-reducing granules, at first separate, appear, gradually uniting to form a fatty envelope which entirely surrounds the structures producing them.

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#### A Comparative Study of the Hydrolysis of Casein and Deaminized Casein by Proteolytic Enzymes.

Max S. Dunn and Howard B. Lewis, *J. Biol. Chem.*, 49:343, Dec., 1921.

In the proteolytic studies of this investigation the action of pepsin, trypsin, and erepsin alone and in series was studied. For the determination of the total amino-nitrogen available on complete hydrolysis, samples of casein and deaminized casein were hydrolyzed according to the method of Henriques and Gjeldbak, but the total amino-nitrogen was determined by the nitrous acid method of Van Slyke. From this figure, the free amino-nitrogen of the intact protein molecule was subtracted and the resulting figure was considered to represent the amino-nitrogen in peptid linkage, i. e., the maximum amount of amino-nitrogen actually available for liberation by enzymes. The liberation of amino-nitrogen during digestion was followed by means of the Van Slyke micro-apparatus. Control experiments were carried out with the same amounts of protein and reagents, but using boiled enzyme solutions. The tabulated results show that casein and deaminized

casein were digested in vitro by pepsin and trypsin. Erepsin digested casein readily but attacked deaminized casein only after the preliminary action of pepsin or trypsin. In every case the digestion of deaminized casein proceeded at a slower rate than the digestion of casein.

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**The Action of Nitrous Acid on Casein.**

*Max S. Dunn and Howard B. Lewis, J. Biol. Chem., 49:327, Dec., 1921.*

In studying the product formed by the treatment of proteins with nitrous acid, since casein is easily obtained pure and its deamination product is insoluble, this protein was chosen for a study of the effect of deamination on the properties and composition of the protein molecule. Pure casein was prepared according to the procedure of Van Slyke and Bosworth, omitting the treatment with ammonium oxalate. The following procedure is superior to the methods outlined by Levites and Skraup for the preparation of deaminized casein: 100 gm. casein are added to 2 liters distilled water contained in a 5 liter pyrex flask. After stirring vigorously for thirty minutes with a mechanical stirrer a uniform suspension of the protein results. To this suspension 140 c.c. glacial acetic acid are added dropwise, with continual stirring, during the course of one and a half hours. At the expiration of twenty minutes a good emulsion is formed, while at the end of the period, solution is effected. To this solution, 500 c.c. of a solution of sodium nitrite containing 80 gm. to the liter are added dropwise, with continued stirring, during the period of one and a half hours. After 150 c.c. of this solution have been added, a deep yellow precipitate rises to the top of the liquid as a yellow layer which, after standing for eighteen hours, is filtered on a Buchner funnel by suction, with a hardened filter paper. After triturating this substance fifteen times with hot water to the disappearance of an acid reaction to litmus, it was found to be granular and light yellow in color while the aqueous filtrate was similarly colored. The yellow precipitate obtained by triturating four times with 95% alcohol was thoroughly desiccated by triturating three times with dry ether, drying in air for thirty minutes, and in the oven at 80° C. for an equal length of time. Although the alcoholic filtrate was highly colored, the precipitate lost but little of its yellow color in the washing process. The deaminized product was of a uniform color and appearance and it was possible to secure practically a complete transformation into the deaminized form. From three 100 gm. samples of the original casein, yields of 90, 95, and 97.5 gm. of the oven-dried products were obtained.

Tyrosin was isolated from the hydrolysis products of deaminized casein. Quantitative determinations of tyrosin in casein and deaminized casein showed that tyrosin was partially destroyed in the process of deamination. The distribution of nitrogen in casein and deaminized casein was determined by the Van Slyke partition method. In harmony with the current theory as to the nature of the free amino groups of the protein molecule, deaminized casein was found to contain no lysin. The mono-amino-nitrogen of the filtrate of deaminized casein was increased, the increase being nearly proportional to the decrease in lysin nitrogen. No other notable differences between casein and deaminized casein were found.

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**Amount of Creatin in Human Cardiac Muscle in Various Pathologic Conditions.**

*Fr. Constabel, Biochem. Ztschr., 122:152, Berlin, Sept. 26, 1921.*

Clinical interest attaches to the question whether dilatation of the human cardiac muscle depends on the contractile power and the working conditions, or whether the tonus is independent of the state of contraction. Observations show that in muscles possessing increased tonicity creatins are found in increased amount. By some authors, however, this conclusion is disputed. The amount of creatin in the hearts taken from 38 corpses was determined. In normal hearts 1.7-1.8 mg. of creatin was found in each gram of muscle substance. In fatty degeneration of the cardiac muscle, cachexia, and carcinoma, the values decreased (0.6-1.2). Generally, the values in the left and right ventricle agreed to within 10%, but in aortic insufficiency with hypertrophy the figures were 1.60 and 1.28 respectively. Age and sex had no apparent influence. Thus, cardiac muscle in good tense condition gave a high creatin value, in flaccid condition and in fatty degeneration, a low creatin value.

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**Simple Exact Method for the Direct Simultaneous Estimation of Acetaldehyd and Acetone.**

*Wilhelm Stepp and Robert Fricke, Hoppe-Seyler's Ztschr. f. physiol. Chem., 116:293, Berlin, Oct. 22, 1921.*

The usual methods of determining acetone and acetaldehyd being imperfect, the Tollens reaction for aldehyds was elaborated for quantitative determination. The method is as follows: To the fluid containing aldehyd, is added an excess of ammoniacal silver-solution of known titer; the mixture is allowed to stand in the cold for several hours, then heated for a few minutes at the return condensor. After filtering from the reduced silver and over-acidifying the filtrate, the unused silver is titrated with ammonium thiocyanate and ferric ammonium sulphate. The titer is exact to the milligram.

The acetone is determined after removing the aldehyd by boiling with silver oxid or Fehling's solution at the return condensor; it is distilled off and the acetone determined by the iodin combination.

Aldehyd and acetone are determined simultaneously by combining both methods. The solution to be tested is mixed with a freshly prepared suspension of silver oxid of known strength, allowed to stand for several hours, and boiled in the return condensor. The aldehyd is thus oxidized, the acetone is distilled off, the residue dissolved with ammonia, and the aldehyd content titrimetrically determined as above detailed.

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**Formation of Acetaldehyd and Fermentation with Various Fungi.**

*C. Neuberg and C. Cohen, Biochem. Ztschr., 122:204, Berlin, Sept. 26, 1921.*

Formerly, the view predominated that the small amounts of acetaldehyd that may arise in the alcoholic fermentation of sugar do not represent a normal product of fermentation, but are produced through

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the subsequent oxidation of the alcohol in the presence of atmospheric yeast. Now, however, the primary generation of acetaldehyd in various types of biologic splitting of sugar is accepted, as well as the simultaneous formation of definite products of reduction and accumulation.

For the further elucidation of these questions, a series of organisms was investigated, which, by reason of their chemical action, appear partly related to the organisms inducing alcoholic fermentation and are partly responsible for other destructions of carbohydrates. Mucoraceae were employed and quantitative determinations carried out with them. It appeared that the sugar conversion products produced by these organisms (acetaldehyd and glycerin) were present in molecular proportion, while the quantity of spirit formed decreases simultaneously. It was, therefore, proved that acetaldehyd is a material product of metabolism and that it probably plays a part in the animal economy.

Each 100 c.c. of the experimental solution contained 6 gm. grape sugar, 1 gm. monopotassium phosphate, 0.6 gm. magnesium sulphate and 0.6 gm. Witte's peptone. To this, when sterilized was added 100 c.c. of a 6% solution of secondary sodium sulphate that had been rendered sterile by 2 boilings in vacuo. To this mixture, 1 gm. calcium carbonate was added, the whole inoculated with mucor and incubated at 28°. After twenty-four hours, the sodium nitroprussid test for acetaldehyd gave a positive reaction. After eighteen days, HSO was neutralized, CaCO added, and the acetaldehyd distilled off. The amount found was 0.594 gm. aldehyd and 15.08% sugar had disappeared. Glycerin was tested for by extracting the residue after evaporation with alcohol and was found in abundance.

Besides the mucor species, where the effect was determined quantitatively, Aspergillus fumaricus niger, Penicillium variabile, Merutius lacrimans, and also mold yeast, were experimented with. All fungi with decided oxidative metabolism produced acetaldehyd, but apparently used it up again. Anaerobic organisms like the yeasts are capable of enriching already formed aldehyd. Under the influence of absorptives (sodium bisulphite and calcium bisulphites) considerable quantities of glycerin and acetaldehyd are formed correlatively. The fermentation was demonstrable with a number of new microorganisms, such as Mucor javanicus, Mucor plumbens, Mucor racemosus, Monilia condida, Torula colliculosa.

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Formation of Mercapturic Acid during the Albumin Minimum.

*Joseph Kopfhammer, Hoppe-Seyler's Ztschr. f. physiol. Chem., 116:302, Berlin, Oct. 22, 1921.*

Benzene bromid  $C_6H_5Br$  can be excreted as bromophenylmercapturic acid  $BrC_6H_4SCH_2CH(NHCOCH_3)COOH$  and isolated from the urine in beautiful crystals. In it is contained the albumin "building unit" cystein, which the halogens of benzene evidently seek out from the albumin metabolism, to unite with it. Cystein which is formed in the intestine from albumin in the food, is absorbed as such and combines with the benzene halogens by oxydation and acetylation. When, as under the conditions of an albumin minimum, cystein is derived from body albumin, no union takes place. The authors fed a dog on potatoes, later on pure potato starch made into paste and on rendered fat. Within

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eight days, all reserve albumin had been used up and the dog was fed with benzene halogens in gelatine capsules. The urine, which hitherto had shown no mercaturic acid, was precipitated with basic lead acetate and NH<sub>3</sub>; the alcoholic extract of the precipitate, which must contain the mercapturic acid was tested with the thiophenol reaction. It was negative. Thus under the conditions of the albumin minimum no mercapturic acid is eliminated. When the above test was repeated and the dog received, at the same time, a subcutaneous injection of cystein, considerable amounts of mercapturic acid were eliminated, from which it may be inferred that no cystein at all is produced from the used-up organ albumin.

(1b-54)

**Colorimetric Investigations on Tryptophan. VI. The Amount of Tryptophan in Various Foods and the Tryptophan Needs of Adult Human Beings.**

*O. Fürth and F. Lieben, Biochem. Ztschr., 122:58, Berlin, Sept. 26, 1921.*

In order to ascertain the amount of tryptophan required by adults and the satisfaction of this requirement by various diets, the estimation of the exact amount of tryptophan in a number of the most important foods was attempted. Colorimetric estimation was effected quite easily in the case of flesh foods and eggs, weighed quantities of which were extracted with strong warm lye. But this method could not be applied to starchy substances (cereals), fatty materials (such as cheese) and vegetable products poor in tryptophan. In these the separation of the albuminoids had to be done previously in such a manner that the globulin proteins were removed (by extraction with 10% dilute cold saline solution), following which the protamins soluble in alcohol were extracted with warm alcohol. The globulins were precipitated with acetic acid while protamins were precipitated from the alkaline solution by addition of water, and the percentages of tryptophan present in both were estimated. After the globulins (3.1% tryptophan) and protamins (2% tryptophan) in the original material had been calculated, the amount of tryptophan in the latter could be determined. The estimation of tryptophan is preceded by that of the total proteins. In the case of plants with low tryptophan values, green vegetables and potatoes, the proteins are recipitated from the expressed juice by means of acetic acid and coagulation by heat, whence the percentage of tryptophan in the precipitate is estimated.

The amount of tryptophan in adult human beings was calculated from a large number of contributions to the literature on metabolism. The calculations were based on the following types of feeding; (a) normal generous diet; (b) abnormal types of diet; (c) strict vegetarian diet, and (d) albumin minimum experiments without disturbance of N equilibrium. The calculation of the average amount of tryptophan in the nutrient proteins considered the total quantities of raw albumin and pure albumin taken daily, and quantities taken per kilo of body weight per day.

The daily tryptophan requirement of the adult weighing 70 kg. is apparently 2.5-3.2 gm. on a generous and unrestricted diet. This corresponds to 0.035-0.046 gm. per kilo per day. So long as the diet is sufficient and general conditions are favorable, the tryptophan may

be reduced by one-half, viz., to 0.017-0.020 gm. per kilo daily without danger to the individual. The N equilibrium is not immediately destroyed even if the daily supply is reduced to 0.015-0.009 gm. though how long maintenance can continue on such a limited supply is uncertain.

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**The Alcohol-Soluble Protein of the Caryopsis of Sorghum Vulgaris.**

*Sabato Visco, Arch. di farmacol. sper., 31:173, Rome, June 1, 1921.*

Sorghum vulgaris (*andropogon sorghum, olcum sorghum*) is a plant of the family graminæ, genus sorghum, grown in all mild climates. Its fruit is a small caryopsis, reddish-brown in color, which can be ground to a fine brownish powder. All attempts to extract an alcohol soluble protein from this caryopsis, as has been done in the case of most other graminæ, proved futile. T. B. Osborne in 1919 gave the first inkling of the existence of such protein. The fruits of a common variety of sorghum were freed of their glumes and ground to a fine powder which was then passed through a silk sieve. Part of the powder was extracted with 70% alcohol at 60° C. for twelve days, the supernatant fluid being decanted off every three days and fresh alcohol added. The fluid was then mixed with a salt solution, when a yellow precipitate separated out. This was repeatedly washed after filtration; and on the addition of distilled water to the filtrate, a new, white flocculent precipitate was formed which, after drying, became a fine white powder, soluble in alcohol but reprecipitated on the addition of distilled water. The material remaining on the filter was of elastic consistency, like rubber. After drying, it was ground in a mortar, with some difficulty. Tests conducted on both powders showed that they contained a protein (whether absolutely identical could not be determined), presumably of the prolamin group. This amounts to about 3.5% by weight of the powder. The alcohol soluble protein of the caryopsis of sorghum vulgaris—likely to be called sorgchein—has a nitrogen content below that of the other known prolamins (gliadin, hordein, zein), and does not give the Adamkiewicz and the Liebermann reactions, probably—by analogy to zein—on account of lack of the tryptophan molecule.

**1c. PHARMACOLOGY AND TOXICOLOGY**

(1c—49)

**Pharmacology of Vessels. I. The Effect of Poison on the Pulmonary and Large Cutaneous Artery of Rana Esculenta.**

*Leo Adler, Arch. f. exper. Path. u. Pharmakol., 91:81, Leipzig, Oct. 11, 1921.*

The brain and spinal cord of frogs were destroyed, the anterior wall of the chest removed, and a fine glass cannula introduced into the right and left pulmocutaneous artery. This was then tied into the pulmonary artery. The lung was flushed out with Ringer's solution, isotonic with frog's blood (saturated with oxygen), from a height of 30 cm. and contained in a Mariotte flask; 1 c.c. of the substance to be tested was dissolved in Ringer's solution in the afferent rubber tube, and injected. In this manner suprarenin was examined combined with

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inactivated horse serum, lest it be destroyed. Then hystamin, tyramin, phenylethylamin (in concentration of 1:2,000, 1:50,000 and 1:100,000), hordenin (oxyphenylethyldimethylanilin), aqueous nonalbuminous extracts of various organs as thyroid and thymus, pituglandol, peptone and barium chlorid, morphin hydrochlorid, codein phosphate, papaverin hydrochlorid, and narcotin sulphid (1:3,000, 1:300,000, and 1:2,000,000) were injected and the change of the muscles studied. The result of these tests is as follows: Lactic and carbonic acid, both products of catabolism, were able to increase respiration when there is need. Regulation takes place in the living animal by dilatation of the vessels of the lung and skin so soon as a certain acid concentration of the blood develops. The vessels again contract when the concentration drops.

Both the pulmonary and large cutaneous artery of the frog are caused to contract by comparatively large doses of suprarenin, hystamin, tyramin, phenylethylamin, hordenin and pituglandol, and are relaxed by weaker doses. Peptone, papaverin and narcotin, in strong as well as weak concentrations, always cause dilatation. Barium chlorid and soda are vasoconstrictors. Lactic acid and hydrochloric acid in weak concentration and CO<sub>2</sub> in saturated solution cause contraction. The control tests of meat with the same acids, upon the vessels subservient to internal respiration and situated in the posterior extremities of the frog, confirm this; they also confirm the action of the optimal concentration of the products of catabolism (CO<sub>2</sub>).

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**Comparative Researches on Infusions into a Vein of the Systemic Circulation and into the Portal Vein.**

*Motoi Yamada, Biochem, Ztschr., 122:168, Berlin, Sept. 26, 1921.*

The liver acts like a dam in relation to the heart, as a safeguard against too great flooding with fluids. Researches were initiated to ascertain in what way the conditions of circulation are affected by an infusion at one time into the jugular vein and at another time into the portal vein. For these experiments, rabbits and cats were employed. A cannula was tied into the carotid artery and served to measure the blood pressure, while the cannula in the jugular vein was used for infusion. Both vagi were divided. A tracheal cannula was tied in the trachea and after ligation of the celiac artery and the descending aorta another cannula was tied in the main branch of the portal vein. The animals were under morphium-ether narcosis, their body temperature being maintained by incandescent electric lamps. Previous to, and after, each interference, the amount of hemoglobin in the blood was determined. Experiments show that the liver need not necessarily retain the liquid by reason of its structure, inasmuch as a saline infusion into the jugular vein produces no differences in the degree of blood dilution, in contradistinction to saline infusion direct into the portal vein, in which case the liver is excluded from the circulation. If saline infusion into the jugular vein be compared with infusion into the splenic vein—a side branch of the portal vein (under otherwise normal conditions) dilution of the blood is readily observed after infusion. In this arrangement of the experiments, increased excretion of urine takes place after infusion into a branch of the portal vein in spite of the increased dilution of the blood following infusion into the jugular vein. This physiologic fact may rest on increased dilution, or on a

heightened formation of lymph due to an increase in liver function. The state of the blood pressure affords no explanation for these differences.

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**Determination of Alcohol in Solutions.**

*A. Lévéque, Bull. d. sc. pharmacol., 28:549, Paris, Dec., 1921.*

The authors have attempted to utilize the critical temperature of miscibility of alcoholic with other solutions, and to apply the method to the determination of alcohol in alcoholic tinctures. The process described is more sensitive than that recently devised by M. Rosset, and depends upon the principle that turbidity occurs on mixing various solutions. The turbidity occurs always at the same temperature for solutions of the same composition. In one of the solutions consisting of ethyl alcohol, the quantity of the latter may be ascertained by finding the point at which it produces turbidity with various reagents and at various temperatures. The critical temperatures for solutions of alcohol titrating 55, 57.5, 59 and 60 were, respectively, 57°, 41.8°, 32.5° and 26.5°. The curve traced for the figures is practically a straight line. One degree in temperature corresponds to about 0.16 of a titration unit. These figures apply for 0.7 gm. menthol and 5 c.c. of the dilution of alcohol. For alcohol titrating 65 to 70, 2 gm. menthol are used per 5 c.c. of the alcoholic dilution. The critical temperature for titers of 65, 68 and 70 are 62.5°, 41.5° and 27.5°. When the titer lies between 60 and 65, the temperatures may be read by prolonging the curves traced for the previous figures, or 1.2 gm. of menthol may be taken; for titers of 60 and 65, the critical temperatures will be 57° and 23.5°. For titers over 70, other substances are used, (crystallizable benzin, xylol, pure anilin sulphate). For titers below 24, crystallized phenol is suitable. The results obtained by this method are sufficiently exact for practical purposes.

(1c—52)

**Ammonia Excretion Following Experimental Administration of Acids via the Stomach and Peripheral Vein.**

*Robert W. Keeton, J. Biol. Chem., 49:411, Dec., 1921.*

The experiments described in this paper were undertaken for the specific purpose of comparing the relative effects on the ammonia excretion in the urine of acid administration by the alimentary route and by the peripheral vein. Alimentary administration should subject the liver to the effects of a relatively large quantity of free acid, while the latter would afford opportunity for the neutralization of more of the acid in the blood or tissues outside of the liver. In the experiments female dogs of about 16 kilos body weight were used. They were fed a constant diet, consisting of milk, 100-200 c.c.; bread, 50-100 gm.; sodium acetate, 0.5 gm. twice daily at 6.30 a. m. and p. m. To the morning feeding, 100 c.c. of physiological salt solution were added, which served to keep the volume of liquids the same in the experimental and in the control periods. The sodium acetate was given to promote uniform elimination. Collections of urine were made twice daily by catheterization and irrigation of the bladder. The cages were scrubbed and disinfected every twelve hours to prevent decomposition of occasional specimens passed spontaneously. This procedure gave con-

sistent ammonia values. The urines were placed on ice without preservatives, the ammonia and total nitrogen being estimated shortly after the closure of the twenty-four hour period. The ammonia was estimated by means of formalin titration as described by Wiechowski, and checked with Folin's aeration method. The total nitrogen was estimated by the Kjeldahl method, the creatinin according to Folin. On the morning of the experiment, the salt solution was omitted from the diet. The acid was then administered either by the stomach tube or into the leg vein. For the latter, a cannula was inserted into the vein under local anesthesia, and the acid introduced by gravity throughout the period of one hour. The tabulated results show that the administration of 0.1 N HCl by stomach tube to dogs causes an absolute increase in the ammonia nitrogen excreted in the urine, while the total nitrogen remains practically constant. Intravenous administration of the same dose of acid to the same animal causes an increase in excretion of both ammonia and total nitrogen, but the normal ratio between these is fairly well maintained. Alimentary administration of acid is associated with a shift in the nitrogen partition toward the ammonia fraction. Such a shift in nitrogen partition the author found to be absent following intravenous injections if the dose of acid was not too toxic.

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**Commercial Preparations of Javel Water.**

*A. Guillaume, Bull. d. sc. pharmacol., 28:558, Paris, Dec., 1921.*

There is considerable variation in the preparations appearing on the market. The sale is not unaccompanied by fraud. The effectiveness of Javel water depends on its content of chlorin, as expressed in chlorometric degrees (Gay-Lussac). A chlorometric degree is taken as the volume of active chlorin released by 1 liter, at 0° and 760 mm. There is no definite law in France regulating the sale of products of this kind, but the Government has issued several circulars condemning the practice of selling preparations containing too little chlorin. The association of manufacturers has promulgated certain rules applying to designation and sale. Preparations yielding less than 12° per liter should bear a label setting forth the fact. Javel solutions deteriorate with time. The loss is relatively small in preparations of low chlorin content, but variable and relatively great in solutions originally containing much chlorin. The manner of storing is important. The addition of NaCl to Javel solutions is commonly practised on account of its supposed preservative effect; in reality it does not preserve the solutions. On the other hand, the addition of sodium bichromate has a very important preservative influence, since the color produced by it acts like a screen in excluding the actinic light rays. Such use of sodium or potassium bichromate is fully justified.

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**Electrolytic Preparation of Physiologic Solution of Hypochlorite.**

*Gineste and Salles, Compt. rend. Soc. de biol., 85:922, Paris, Nov. 17, 1921.*

Sodium hypochlorite is bactericidal and phagocytic; the Cl is disinfectant, the O regenerative, normal tonus of the serum is maintained and no superfluous or harmful end-products are left. Solutions

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lose two-fifths of their hypochlorite content in twenty-four hours. Their effectiveness depends on the state of the chlorin and oxygen; the latter is most active when the oxygen is nascent. The authors' method supplies, as needed, hypochlorite solution isotonic with blood serum, the temperature being 35 to 38°, and titrating 0.02 per 100 NaClO, or about one-twentieth pure Carrel-Dakin solution; active elements are given off in the nascent condition. A solution of sodium chlorid, of the physiological titer of 5%, is contained in a glass receptacle, with a discharge faucet. The latter is of ebonite or bakelite and has a regulating screw; it also bears two platinum electrodes which are in contact with the solution only at the moment of discharge-flow. The electric current passes between the electrodes, resistance of the solution causing elevation of temperature in the latter (Joule's effect). Any form of current may be utilized by using proper connections. The disinfectant solution is thus always ready and delicate chemical manipulations are avoided.

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**Diuretic Effects of Calcium Salts and the Mechanism of Their Action.**

*L. Blum, E. Aubel and R. Hausknecht, Compt. rend. Soc. de biol., 85:950, Paris, Nov. 17, 1921.*

Sodium, the essential regulator of water exchange in the body, is an intermediate agent; the authors have shown that it is acted upon by potassium. Similarly, it should be acted upon by calcium salts and other substances. A case of generalized edema, refractory to the usual treatment, was studied, calcium salts eliminating water sufficiently to show a loss in body weight of 11 kg. A constant intake of food and liquid was maintained. Most of the calcium was eliminated by the intestine. Observations reported extended over thirty days, calcium chlorid and lactate being given in doses ranging from 2 to 22 gm. Renal elimination of sodium, potassium and calcium is indicated as follows: Sodium: Calcium eliminated sodium, easily at first, gradually with greater difficulty as edema diminished and only in response to increased doses of calcium. Potassium: Small doses of calcium caused retention of potassium, the latter being excreted only when calcium was given in large doses. Calcium: A considerable proportion of calcium was eliminated by the kidneys by reciprocal action of the sodium. Results: Water retention was accompanied by sodium retention; any considerable loss of water was accompanied by excessive elimination of sodium. No direct relation exists between potassium and weight-variation; variation in weight may be accompanied with retention, excessive elimination or equilibrium of potassium. The facts for calcium are the same as for potassium. Charts are given.

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**Antiphlogistic Action of Calcium Salts.**

*L. Blum, Compt. rend. Soc. de biol., 85:1156, Paris, Dec. 17, 1921.*

These experiments were technical and clinical. The technical tests were made in rabbits. If the rabbit is treated previously with calcium chlorid, instillation of a drop of essence of mustard in the conjunctival sac fails to produce inflammation. Intense inflammation, induced in the absence of preliminary treatment with calcium, disappears after

intravenous injection of sufficient doses of calcium chlorid. The simultaneous injection of sodium chlorid and calcium chlorid prevents the effect of the calcium. In inflammations of the serous membranes, fever could be increased at will by giving calcium chlorid, or decreased by giving sodium chlorid. The clinical thus agree with the experimental tests. The mechanism consists of the displacement of sodium and water by calcium, with consequent withdrawal of elements necessary for inflammatory processes.

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**Modification of the Blood and Other Fluids by Calcium Chlorid.**

*L. Blum, E. Aubel and R. Hausknecht, Compt. rend. Soc. de biol., 85:1159, Paris, Dec. 17, 1921.*

After heavy doses of calcium chlorid, given in exophthalmic goiter, nephritis with edema, ascites due to tricuspid insufficiency, lobar pneumonia, grippal bronchopneumonia, and to the normal rabbit (the latter injected also with sodium chlorid), determinations were made for Na, K, Ca and Mg. Conclusions: When renal elimination is active and there is no retention of sodium through edema or inflammation, calcium chlorid diminishes sodium in the blood, in man and the rabbit. Potassium may be increased or diminished; the cause is unknown. When sodium chlorid is retained on account of inflammation, as in pneumonia, sodium becomes increased in the blood with recovery of the normal equilibrium. When renal elimination is retarded, as in asystole with ascites, equilibrium is established between the blood and ascitic fluid. Na passes from blood to fluid as long as calcium is given. When it ceases, Na passes back to the blood. Similar facts obtain for Ca. In the body fluids, there is an antagonism between Ca and Na like that observed between K and Na, which causes modification in the mineral content, Na being displaced.

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**The Paradoxical Effect of Potassium on the Rabbit Heart.**

*H. Busquet, Compt. rend. Soc. de biol., 85:1142, Paris, Dec. 17, 1921.*

The temporary arrest of the beat described for the frog heart, was obtained in the isolated rabbit heart by the following procedure: Coronary circulation was maintained by Pachon's perfusor. Two liquids were used, in succession. The first was a Ringer-Locke solution without potassium, the second the regular Ringer-Locke solution also containing 0.20 gm. KCl per 1000. After the second liquid has been passing for a few seconds, the ventricles are arrested in diastole, the auricles continuing to beat feebly. The ventricular arrest lasts two to three minutes, suspension of the contraction being due to the potassium. For good demonstration, the heart should be in good condition and not exhausted by previous work or exposure to toxic agents. The arrest is not caused by potassium intoxication, but resembles the arrest produced by stimulation of the vagus. It occurs after paralysis of the cardio-inhibitory apparatus and is due to direct action on the cardiac muscle.

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**Chemical Composition of Belladonna Leaves.**

*A. Goris and A. Laronneau, Bull d. sc. pharmacol., 28:499, Paris, Nov., 1921.*

Attempts were made to isolate volatile alkaloids. Bases, in the form of sulphates, were obtained from 500 kg. belladonna leaves. In aqueous solution, the sulphates were treated with sodium carbonate and exhausted with ether. Fixed and volatile alkaloids were removed, with a small quantity of volatile, fatty amines, most of the latter remaining in the watery solution. The ethereal solution was well washed, to remove amines; fixed alkaloids crystallized out; the solution was distilled on the water bath and in vacuo; the distillate, collected by refrigeration, has the odor of pyridin and reddens phenolphthalein; pyridin is present (not over 2%). Distillation in 3 fractions ( $80^{\circ}$  to  $90^{\circ}$ ,  $90^{\circ}$  to  $100^{\circ}$  and over  $100^{\circ}$ ) gives the second fraction as richest in pyrrolic compounds. A portion was treated with hydrochloric acid, the resulting chlorids being precipitated with  $\text{AuCl}_3$  and crystallized fractionally, 2 chloroaurates being separated, with melting points of  $190^{\circ}$  and  $215^{\circ}$  C. (N-methyl-pyrrolin and N-methyl-pyrrolidin). Liebermann's test for unsubstituted nitrogen pyrrolic bases could not be obtained. Washings of ether, and the original aqueous residue, were again washed with ether to remove pyridic or pyrrolic compounds, and distilled in vacuo, the distillate being collected in dilute HCl. Evaporation yields a deliquescent chlorid; treated with soda, the latter gives off a spermatic, tobacco-like odor and yields a fairly soluble chloroaurate, melting at about  $200^{\circ}$  C. Silicotungstic acid is the best reagent here, since it is not affected by the ammonia which always accompanies amines. (For testing traces of ammonia in presence of amines, amin chlorids are first dried, then dissolved in absolute alcohol. The solution, treated by a fresh solution of oxalic acid in absolute alcohol, forms a crystalline precipitate of ammonium oxalate in the presence of ammonia. Excess of amin prevents this reaction, which permits determination of 0.002 of ammonium chlorid in presence of 0.10 amin chlorids). Heating the chlorid with HCl yields vapors coloring red a pine splinter moistened with HCl. A diamine of pyrrolic nucleus is therefore present, containing 4 C atoms, or with 2 N atoms united with 2 C atoms in the 1-4 position. Tests for tetramethyldiaminobutane were negative. Amin from the original solution, ammonia-free, was precipitated as silicotungstate, but the amines were lost by treatment with soda and distillation. Substances found were therefore pyridin, N-methyl-pyrrolin, N-methyl-pyrrolidin and an unknown fatty diamine in the 1-4 position. The Codex method determines volatile and fixed bases combined. To the resulting error, another must be added; bases of small molecular weight are expressed in terms of atropin, whose molecular weight is high; the final result states a weight of alkaloid greater than the sum of fixed and volatile alkaloids of the plant.

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**The Nature of the Alkaloids of Belladonna Extracts.**

*A. Goris and P. Costy, Bull. d. sc. pharmacol., 28:545, Paris, Dec., 1921.*

Belladonna leaves contain much more hyoscyamin than atropin. Physiologically, hyoscyamin is twice as active as atropin. It is generally  
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granted that the activity of a given quantity of belladonna extract is too great to be due solely to atropin. The presence of hyoscyamin explains his fact. In order to learn to what degree hyoscyamin undergoes transformation during the process of extraction, various watery and alcoholic extracts were prepared from belladonna leaves. Each extract was tested for humidity, quantity of total alkaloid (by the method of the French Codex) and rotatory effect of the alkaloid isolated. The dextrorotation obtained was  $14^{\circ} 15'$  for an extract evaporated on the water-bath;  $18^{\circ} 26'$  for an extract evaporated by heat, in vacuo;  $19^{\circ} 32'$  for an extract evaporated in the cold and in vacuo;  $20^{\circ} 10'$  was the index of unextracted belladonna leaves. If no heat is employed, the alkaloid remains substantially as in the untreated leaves. The hyoscyamin remains unaltered in proportion as heat is absent, which is very important from the standpoint of physiological activity. Alcoholic extracts are superior to aqueous extracts. The French process is practically correct; the heat should be diminished by using a sufficient vacuum. The Dutch and Belgian pharmacopeias are right in assigning low temperature limits (respectively  $80^{\circ}$  and  $50^{\circ}$  C.) for the preparation of belladonna extracts.

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**Pharmacologic Analyses of Belladonna and Digitalis.**

*Luigi Alessandri, Arch. di farmacol. sper., 31:143,115, Rome, May 1, 15, 1921.*

Several samples of leaves of *Atropa Belladonna* and *Digitalis purpurea* grown in the province of Florence (Italy) were examined with a view to determining their pharmacologic action. The method employed in the case of belladonna was that of Caesar and Loretz, providing for the weighing of the ether-extracted alkaloids and their titration with tenth-normal hydrochloric acid, using hematoxylin as an indicator. The comparative results obtained indicate that the transplantation of belladonna, especially into non-mountainous regions, does not encourage a favorable development of the plant from a pharmacologic standpoint; that leaves from plants growing in mountainous regions, gathered at the proper time and carefully dried and kept, are equal to the imported product both for pharmaceutical and industrial purposes. The digitalis leaves were tested physiologically (amount of drug and period of time required to cause stoppage in systole of a frog's heart). The best results were obtained with leaves from plants allowed to grow in the soil where originally sown, despite the fact that in this case, the plants had been grown quite close together, had not therefore developed well, and the leaves were close to the root. Leaves from transplanted domestic specimens, as well as those from plants transplanted on local soil from plants grown with foreign seeds, proved much less active.

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**Atropin Effects and Chloroform Shock in Relation to the Vagus Nerve.**

*L. Garrelon, A. Leleu and R. Thuillant, Compt. rend. Soc. de biol., 85:1013, Paris, Dec. 3, 1921.*

Cardiac reactions were employed to test the activity of atropin. Without previous section of the nerve, the phase of hyperexcitability was followed, after a long time, by cardiac inhibition. This reaction

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was constant, whether solutions were old or fresh. Further study was made in rabbits, cardiac reactions being recorded by Ludwig's manometer. Stimulation was produced by a moderate current, invariable for each test and controlled by a Dubois-Reymond switch. The vagus nerve was stimulated at the peripheral end and in continuity, after injection of atropin. During a variable time after injection, while no inhibition is produced by stimulation of the peripheral end of the nerve, stimulation applied in continuity to the other and intact vagus is followed by cardiac arrest. At first very distinct, the inhibition gradually fades, disappearing about an hour after the time of injection. To obtain these results, the optimal dose of atropin injected intravenously into the rabbit is 2 mg. The tests show that stimulation of the intact vagus is modified by passage through the bulbar centers; the reaction is reinforced, since cardiac inhibition remains until the atropin can affect the centers. Cardiac reactions following peripheral stimuli which reach the medulla were also examined. Tests were made in the rabbit because of its sensitivity to chloroform and ease of registering Roger's cardiorespiratory reflex. After injection of atropin, the cardiac shock due to chloroform coexisted with the inhibition following stimulation of the intact vagus; it ceased a little before disappearance of the inhibition. The experiments indicate why chloroform may suddenly arrest the heart in individuals whose vagus is hypersensitive. They also explain the action of atropin injected to prevent vagus inhibition of the heart. Neither intravenous, nor subcutaneous, injections of adrenalin prevented the cardiorespiratory reflex.

(1c—63)

**Gastric Effects of Atropin and Pilocarpin in Endocrine Disturbances.**

*F. Durant, Arch. di farmacol. sper., 31:135, Rome, May 1, 1921.*

The endocrine changes were induced artificially by the oral administration of adrenal, pituitary, thyroid or pancreatic products; the other drugs were also given by mouth. The subject used for investigation was a man of 25, apparently in good health, with normal gastric function. The changes in gastric secretion and digestive power (the last determined by the amount of gastric filtrate necessary to digest 10 c.c. of a solution containing 1 gm. pure casein, 10 c.c. of 25% hydrochloric acid, distilled water to 1,000 c.c. in two hours) induced by the endocrine substances alone were as follows: Suprarenal extract caused an increase in total acidity, in free HCl and digestive power; thyroid caused a slight increase in free HCl with no change in total acidity or digestive power; pituitary substance caused a general increase in all gastric functions. Atropin alone caused a diminution in total acidity, free HCl and digestive power; pilocarpin alone caused a general increase in all gastric functions. Adrenal substance and atropin, injected in sequence at ten minutes' interval, caused an increase in acidity, but no change in digestive power; adrenal substance and pilocarpin, similarly administered, caused a marked increase in total acidity, free HCl and digestive power. Pituitary extract, followed in ten minutes by atropin, caused a diminution in acidity; pituitary and pilocarpin caused an increase in acidity and digestive power. Thyroid and atropin diminished all gastric activity, whereas thyroid and pilocarpin increased it. Pancreatic tissue with atropin increased acidity and digestive power; pancreas with pilocarpin

caused an even more marked increase in all gastric functions. The pharmacologic action of atropin and pilocarpin on the stomach will therefore vary with any endocrine imbalance present.

(1c—64)

**Test for Small Quantities of Pyridin.**

*A. Goris and A. Larsonneau, Bull. d. sc. pharmacol., 28:497, Paris, Nov., 1921.*

The authors have devised a test for pyridin occurring in small quantities, as in belladonna leaves. Attempts to obtain crystalline compounds with cadmium iodid, mercury chlorid and picric acid were unsuccessful. The successful test depends on the ability of pyridin to combine with anilin in the presence of cyanogen bromid to form a crystallized red coloring matter, melting at 162°, the bromid of alpha-analidophenylidihydropyridinium. This was precipitated in acicular crystals by mixing 1 drop pyridin, 1 drop anilin, 1-2 c.c. water with 5 to 10 cg. freshly prepared cyanogen bromid. The test is very delicate; intense for a solution containing 1 drop pyridin to 250 c.c. and still more distinct for an aqueous solution containing 1 drop pyridin to 10 liters. The color is at first yellow, becoming orange in thirty to forty minutes; red, oily droplets are formed in twenty-four to forty-eight hours. The test is specific, being negative for pure distilled water and with pyrrolic derivatives, especially with 2-methyl-pyrrolidin; it permits detection of pyridin in presence of pyrrolic bases; it is satisfactory for belladonna leaves.

(1c—65)

**Action of Veratrin on Normal and Degenerating Muscles in Amphibians.**

*J. Fontes, Compt. rend. Soc. de biol., 85:1171, Paris, Dec. 17, 1921.*

The results obtained with the gastrocnemius and hyoglossus of the frog have been reported. Further investigations have followed, the action of veratrin on the gastrocnemius of the toad (*Bufo vulgaris*) and the degenerating gastrocnemius of the frog. A 1:1000 solution of veratrin was employed. As the intoxication increases, the curve approaches the form of that called the "Funcke's nose." The effect produced does not correspond to that shown by the frog's gastrocnemius, but to the result appearing in the frog's hyoglossus. No interpretation of the curve is attempted. The author suggests that the results depend on the fact that the frog's gastrocnemius produces rapid contractions, while the frog's hyoglossus and the toad's gastrocnemius are alike in producing slow movement. As long as the nerve of the frog's gastrocnemius remains attached to the muscle, the veratrin curve never exceeds that of the first tracing, but if the preparation is allowed to degenerate for several days, the curve obtained resembles that of the toad's hyoglossus and gastrocnemius. Similar curves have been obtained with muscles grafted into the dorsal lymph sac of the frog.

(1c—66)

**The Antispasmodic Action of Black Horehound (*Ballota* *Fetida*).**

*H. Leclerc, Bull. d. sc. pharmacol., 28:554, Paris, Dec., 1921.*

This plant, although neglected, is very useful. It is common all  
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over France, but grows especially along the roadsides. It was formerly considered good for a number of conditions, including application as a wound dressing and use in the treatment of nervous symptoms. The author summarizes the botanical features. He has observed beneficial results from its use in the treatment of nervous symptoms in an individual susceptible to suggestion, in neurosis due to suppressed menstruation, in disturbances of the menopause and in a case of psycho-neurosis accompanied by marked agoraphobia. He used it with good effect in an epidemic of pertussis; here the dose was 20 drops of an alcoholic infusion per day.

(1c—67)

**The Gum of *Entada Sudanica*.**

*L. Raybaud, Compt. rend. Soc. de biol., 85:933, Paris, Nov. 17, 1921.*

The plant producing this gum is a small shrub, subfamily Mimoso (Adenantherae) occurring in French Equatorial Africa. The gum occurs in fine filaments; it is yellowish-amber, clear, sometimes brown-veined, and strongly adherent to the bark. Solubilities and reactions to lead, copper, potash, stannous and mercurous chlorids, iron perchlorid and acetic acid are described. It is found that 92% of the gum is soluble in cold water, the remainder being a tragacanthous or mucilaginous gum. If this insoluble portion be heated for twenty-four hours in 50 times its volume of water, it becomes almost entirely converted into soluble gum, which, after drying, loses the property of swelling. The permanently insoluble portion consists of cellulose débris, staining red with carmin, and a small quantity of a gelatinous material refractory to all stains. Pectinic substances and a reducing sugar are present; starch is absent. The presence of reducing sugar and of tragacanthous gum distinguishes the article from a true gum and diminishes its commercial value.

(1c—68)

**The Box Thorn (*Lycium Vulgare Dunal*) and Its Botanic, Chemical and Pharmacologic Relations.**

*R. Weitz, Bull. d. sc. pharmacol., 28:503, 562, Paris, Nov.-Dec., 1921.*

The plant is solanaceous and usually designated as *Lycium barbarum* L. The species named in the title is most widely distributed in central and western Europe. Differences between *L. vulgare* and *L. barbarum* are listed. Its origin appears to have been western Asia. The plant occurs semiwild in North Africa and southern Europe and on coasts of the Channel and North Sea, nearly always near towns and in hedges. Root, stem, leaf, flower, fruit and seed are described in detail. Granules of calcium oxalate occur in the root, stem and leaves. In the Orient, Spain and Provence, leaves and young shoots are used as salad, and teas and decoctions are made from them. In Spain and Portugal, the plant is used in the treatment of pertussis, its usefulness being confirmed by Galavielle of Montpellier. In Macedonia, infusions mixed with infusions of fruit of a fraxinella are used as a home remedy for infantile diarrhea. Various therapeutic applications are made in China, Indo-China and Japan, of the leaves, fruit and bark.

The alkaloid of this plant, as well as of *Lycium barbarum*, lycin, (Sec. 1—Page 278)

is the same as the alkaloid betain of the beet. Weitz summarizes its chemical reactions. A mydriatic alkaloid was not found in the plant. Cholin appears to accompany betain, but solanin and other organic bases are absent. Leafy twigs, collected in summer, contain about 80% water, 2.16% ash, and yield 3% moist alcoholic extract. The analysis of the dried material shows 10% ash and 68% organic matter, of which 2.5% is reducing sugar. The high ash is considered due to calcium salts. Dogs are more sensitive than rabbits to the alkaloid. The extract appears readily diffusible within the organism. Injected into the cellular tissue, the extract is irritant and escharotic, like trimethylamin and betain. Intoxication symptoms produced in the guinea-pig and rabbit consist of a phase of transitory agitation, uneasiness, hebetude, spasms, insensibility, paralysis and death. The same symptoms appear in the dog, also vomiting and salivation. The heart is arrested in diastole; sometimes it cannot be stimulated, sometimes a few fibrillary contractions may be produced. Intravenous injection of less than 1 cg. per kilo body weight, of the extract, causes abrupt fall of the carotid pressure. A somewhat larger quantity produces a reduction in the volume of the kidney, probably resulting from vasodilatation in other organs; 20 to 25 cg. per kilo weight paralyzes the vagus; a still greater quantity produces almost instant death, with maximum constriction of the kidney. The cardiac rhythm of the frog is slowed and the systolic duration prolonged. The drug acts most distinctly as a cardiovascular depressant. Lycium is brought within the atropin group on account of its production of paralysis of the vagus. These reactions are not produced by betain alone. Another substance, probably of the cholin group, is doubtless present in the plant.

(1c—69)

**On the Action of Radix Ginseng on Experimental Hyperglycemia**

*Itohei Saito, Japan Med. World, 1:3, Tokio, Nov. 15, 1921.*

Radix ginseng is the root of *Panax ginseng*. Its medicinal value has been believed to be only that of a demulcent. It has, however, a wonderful reputation in the Orient, having been used for a long time as a home remedy in a variety of ailments. Saito has previously reported that it is superior to other drugs in its suppressive action upon experimental and dietetic glycosurias produced by adrenalin and grape sugar. Using these again, he experimented with the drug in hyperglycemia. Bang's quantitative determination of blood sugar was employed. Ginseng powder, in water, did not give uniform results because it was not readily absorbed. When the extract was injected subcutaneously (in rabbits) or given by mouth, it prevented adrenalin hyperglycemia. When the hyperglycemia was produced by feeding sugar, the addition of ginseng extract, in the ratio of 2 gm. per kilo of animal body weight, brought the blood sugar back to normal and the sugar in the urine disappeared. Experiments are detailed, with charts showing the sugar curve.

(1c—70)

**The Methyl Alcohol in Arsphenamin (Salvarsan).**

*Philip Adolph Kober, J. Lab. & Clin. Med., 7:168, Dec., 1921.*

Kober pointed out before that there is no valid reason for assuming  
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that Ehrlich's preparation of arsphenamin contained two molecules of water of crystallization, which assumption was invoked to account for the arsenic content of 31.6% instead of 34.4% which would be theoretically right for the pure dry drug. He also described a method for preparing a methyl alcohol free arsphenamin from aqueous solution. His conclusions have been disputed by various investigators. One criticism was that a methyl alcohol free arsphenamin is not the product with which Ehrlich did his work on spirochetes, the assumption being that Ehrlich did all his fundamental work with the dihydrochlorid of the salvarsan base, namely "606." But Ehrlich made his fundamental experiments with "592," the salvarsan base. Therefore, the arsphenamin preparation which yields on neutralization the pure and original base, that is, a methyl alcohol free arsphenamin, is not (as was contended) a new drug of unknown therapeutic power. Another criticism was that no methyl alcohol is present in Ehrlich's preparation or in arsphenamin made according to his method. Meyer reported that he had dried large quantities of the Metz preparation and found appreciable water, but only traces of hydrochloric acid and methyl alcohol. But Meyer stated to the author that his method of determining methyl alcohol was a trade secret.

The Metz product is claimed to be identical with Ehrlich's salvarsan and should, therefore, be made with methyl alcohol and ether. This product can give off water only if the methyl alcohol combines with arsphenamin to form methylated arsphenamin, water occurring in the reaction. Fargher and Pyman also concluded that salvarsan contains no free or combined methyl alcohol, but Kober suspects that, owing to excessive drying, the methyl alcohol became attached to the arsphenamin molecule.

He finds that arsphenamin made after Ehrlich's directions does contain methyl alcohol as is indicated by the following facts: (1) Ehrlich found methyl alcohol, by qualitative and quantitative methods, in one of his batches. (2) Rieger got a "strong Mulliken and Scudder" methyl alcohol reaction from samples of German and American salvarsan and from diarsonal. (3) Repeatedly Kober found methyl alcohol and other organic solvents in arsphenamin made by Ehrlich's method, even after reprecipitation with hydrochloric acid, and a methyl alcohol reaction on distillation from an aqueous solution. (4) Methyl alcohol was found in arsphenamin by Raiziss. (5) When precipitated from absolute methyl alcohol and anhydrous ether, arsphenamin seems to lack opportunity to contain water. From these it may be concluded that Ehrlich's salvarsan contains one molecule of methyl alcohol, free or combined, depending on the freedom from water in the materials and on the amount of drying during preparation.

As to toxicity, since a molecule of methyl alcohol would constitute about 7%, there would be about 42 mg. in a dose of 0.6 gm. For free methyl alcohol, unless salvarsan is injected very frequently, or unless complications exist, this amount is not likely to be important. If the methyl alcohol is combined, the toxicity is likely to be greater. Ehrlich and his collaborators made methyl derivatives of arsphenamin and found them very toxic and therapeutically ineffective. Rieger also found that arsphenamin may contain an arseniurated methyl compound which decomposes in the ampules, or on solution, with liberation of arsenous oxid or a cacodyl-like substance, and that, according to the amounts

accumulated, the size of the dose, and the idiosyncrasy of the patient, the reaction may be marked by fall in blood pressure, dyspnea and cyanosis. He thinks that reduction to metallic arsenic by the tissues may occur too readily for safety with the present commercial preparations of arsphenamin.

Kober also considers methyl alcohol and ether unsuitable for treating arsphenamin because they are likely to act as catalysts, giving rise to oxidation or other changes in constitution. Toxicity has been gradually reduced owing to increased skill in manufacturing, especially through working at low temperatures in absence of air. But manufacturers find at times that their product is too toxic for use, without knowing what has caused the excessive toxicity. Kober finds that this does not happen if arsphenamin is made without methyl alcohol and ether. With the hydrochloric acid method he is always able to obtain arsphenamin purer than the U. S. Public Health Service standard, which is 100 mg. per kilo of white rats. Christiansen has been able to get an average of 140 mg. toleration with the hydrochloric acid method, and Nurenberg gets from 130 to 140 mg. toleration by working over old toxic batches.

Especially pure arsphenamin does not dissolve readily in cold water, but first gelatinizes. In warm water the gel dissolves rapidly. This has been noted by a number of workers. After solution in water arsphenamin should be quickly and properly neutralized, so that the alkaline solution is not long in contact with air, a circumstance which has been shown by Roth to increase its toxicity. In solution, very pure arsphenamin is a light straw color. Rapidity of solution should not be sought at the expense of altering its chemical constitution.

(1c-71)

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**Spontaneous Chronic Meningo-Encephalitis of Rabbits.**

*Jean Oliver, J. Infect. Dis., 30:91, Jan., 1922.*

In examining a number of rabbits to study the reactions following arsphenamin administration, Oliver found, in the brain, a peculiar inflammatory process which seemed to have no relation to the drug. Supposedly normal rabbits from the laboratory stock as well as rabbits from the public markets were, therefore, killed and the brains examined, and it was found that about 20% showed the same microscopical lesions, most frequently in the cerebral cortex, but also in the neighborhood of the basal ganglia and the medulla. The lesions were not accompanied by functional disturbances and there was no history of snuffles. Although the disease appears to be of little importance in relation to the general health of the rabbit, the possibility that it may be a source of confusion in experimental procedures is obvious, especially as the affected animals rarely die and there is no simple means of determining from a clinical examination whether the animal is healthy or not.

(1c-72)

(1c-72)

**The Limits of Chemotherapeutic Action of Arsenobenzol Derivatives in Hog-Erysipelas, as Compared with the Effects of Hog-Erysipelas Serum.**

*W. Kolle and H. Schlossberger, Münch. med. Wchnschr., 68:1439, Nov. 11, 1921.*

Negative results were obtained when certain dyes and arsenobenzol  
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derivatives which are effective in trypanosome and spirochete infections, were tested for their therapeutic value in experimental hog-erysipelas in mice.. A few arsenobenzol derivatives formed an exception. Salvarsan and neosalvarsan, as well as their metallic salts, were effective only when used very early in the disease and in doses which approached the limit of toleration. Arsenobenzol derivatives with 4, 5 or 6 amino groups, notably hexamino-arsenobenzol, exerted a distinct curative action on experimental hog-erysipelas in mice.

As soon as the bacteria are demonstrable in the circulating blood, neither erysipelas serum nor the benzol derivatives exert any curative action. This is a remarkable congruence of chemotherapeutic and of sero-therapeutic agents. Substances effective *in vivo* had little or no germicidal action in the test-tube experiment, although they inhibited bacterial growth. On the other hand, none of the substances which, *in vitro*, had a powerful germicidal or inhibitory effect, was able to delay the infection or cure it after it had taken place.

This shows that the effect of the amino-arsenobenzol derivatives in experimental hog-erysipelas of mice is a purely chemotherapeutic phenomenon, there being a distinct difference between a curative dose and the dose of toleration. The animal organism furnishes the antibodies which directly or indirectly cause the death of the erysipelas bacilli *in vivo*.

The chemotherapeutic study of one bacterial infection does not justify one in drawing conclusions regarding another. Nevertheless the experiments here reported open up a possibility of finding other compounds of the arsenobenzol group which, when used early, may exert an action upon the causative agents of infection.

(1c—73)

(1c—73)

#### Active Anaphylaxis Produced by Arsenobenzenes in the Guinea-Pig.

C. Flandin and A. Tzanck, *Compt. rend. Soc. de biol.*, 85:993, Paris, Nov. 26, 1921.

Symptoms induced by arsenobenzenes are not of the same order or pathogeny. Occurring in syphilis, they may be attributed to the treponema; a second group depends on variations in preparing the arsenobenzenes used for treatment; a third group is related to sensitization.. Hitherto, resulting symptoms have not been proved anaphylactic. If a 200 or 300 gm. guinea-pig be given an injection of 2 cg. sulph-arsenol in the heart cavities no symptoms occur if injection is not too rapid; or at most, the animal remains motionless, curled up and appearing fatigued. A second intracardiac injection, made not less than three days later, and of one-tenth to one-twentieth the first dose, induces an anaphylactic crisis in two minutes; the animal remains motionless, and paresis of the posterior muscles appears, or even paraplegia; the animal violently scratches its muzzle, passes urine and feces, becomes agitated, coughs, twists about and is then attacked with spasms, which are sometimes so violent that the animal is thrown about at every contraction. After 20 to 30 spasms, the symptoms decline and the animal appears fully restored. These anaphylactic symptoms may be severe or benign; but even when most violent and with complete paraplegia, they do not cause death. The brevity of the period required to induce the anaphylactic state (three days instead of eleven) differentiates the anaphylaxis (Sec. 1—Page 282)

of arsenobenzenes from serum anaphylaxis. Active anaphylaxis may be induced with arsenobenzenes; a recently described test for passive anaphylaxis permits recognition of arsenobenzene anaphylaxis.

(1c-74)

**Treatment of Experimental Trypanosomiasis with Acids of Arsenic.**

*A. Navarro, Compt. rend. Soc. de biol., 85:976, Paris, Nov. 26, 1921.*

Arsenic acids have been neglected, arsenious acid having received most attention; the former has appeared to be specially toxic to the nervous system. With a view to better definition of values, certain pentavalent arsenical compounds have been studied: 189 (the sodium salt of the acid 3-amino-4-oxyphenylarsenate); 190 (sodium acetyl-aminoöxyphenyl arsenate); 199 (urea of sodium aminoöxyphenyl arsenate); 187 (sodium acid arsenic phenyl acetate); 188 (hydrochlorate of acid arsenic benzylidemethylamin); and 201 (sodium salt of the benzarsenic amid of aminophenylacetic acid). These substances were tested in dancing mice, the tolerated dose being that which produced no unfavorable nervous symptoms. The trypanosomes studied were *T. brucei* (nagana) and *T. rhodesiense*. Product 189 proved most effective. The lethal dose was about 0.04 gm. *T. brucei* kills the mice in four days. The effective dose of the arsenic compound is 7 mg., several cures being obtained with 4 mg. Subcutaneous injections of a 1:8 solution were given. *T. rhodesiense* kills the mice in twenty to thirty days. The effective dose was the same as for *T. brucei*. The maximum dose tolerated was 0.035 gm. The chemotherapeutic coefficient,  $C \div T$  ( $C$ , curative dose,  $T$ , tolerated dose), is one-fifth. This is more favorable than that of atoxyl (one-half) or arsenophenylglycine (one-third). The production of nervous symptoms in dancing mice requires a dose 5 to 6 times greater than the curative dosage. Injection is painless and without necrosis or edema. Results obtained with the other compounds are summarized; all are much inferior to 189.

(1c-75)

**Distomiasis Treated by Intravenous Injection of Tartar Emetic.**

*P. Mauriac and R. Boyer, Compt. rend. Soc. de biol., 85:917, Paris, Nov. 17, 1921.*

Injections were made in 4 sheep whose stools contained ova of two distomas and strongylus. No effect was produced. The conclusion is confirmed by clinical study of a young woman harboring *Fasciola hepatica*. Emetin, thymol, novarsenobenzol and male fern were ineffective. Ten injections of tartar emetic, progressing from 1 to 9 cg., totalling 60 cg., were given in ten days. Toxic effects were induced by 7 cg., more markedly by the last dose of 9 cg.; pain at the site of injection and along vessels of the arm, cough, anguish, pallor, nausea, diarrhea, pulse 150, small and thready. Symptoms disappeared after ten minutes with no sequels. Ova of the parasite appeared unaffected. Injections were repeated in three weeks, no dose exceeding 8 cg., the total being 75 cg. Ova were still unaffected and the patient died five months from date of first injections. Ova of distoma must be sought by continuous and prolonged stool-examination, since they are intermittently absent from the stools.

(1c-75)

(1c-76)

**Use of Potassium Ferrocyanid as an Insecticide.**

*L. Raybaud, Compt. rend. Soc. de biol., 85:935, Paris, Nov. 17, 1921.*

This substance has been used in California for destruction of the cochineal insect (*Icerya purchasi*) on *Spartium junceum* and peach-tree. The insect is found on chrysanthemums in France. The process of introducing a small quantity of the salt within a minute cavity made in the trunk is reported to be successful. The author has applied the method to fig-trees of Provence. The trees are infested with a trapezoidal louse (*Cereoplautes rusci* or *Kermes caricæ*), whose presence favors that of another parasite (*Fumagines*). The latter subsist on the excreta of the former and injure the tree; eradication of the insects facilitates destruction of the fungus. A tubular cavity 10 to 30 mm. in diameter, with a depth of 60 to 150 mm., was made in the trunk, at the height of a man, the diameter of the trunk at such a height being 150 to 300 mm. Some cavities were completely filled with the salt, some only partially filled. All cavities were stoppered with wood or cork. A bluish liquid escaped from the wound in the tree. The leaves of small branches which had suffered from the parasite became necrotic a few days after the operation. The buds lost vitality, becoming entirely dried up the following year, the branches appearing dead. Those in other parts of the tree did not appear to suffer. The larger branches remained vigorous. The death of the smaller branches is due to the toxicity of the ferrocyanid. The tree seems to react. The process was tried for two consecutive years, results being identical at Grasse and in the botanical garden of the laboratory. Crystallized potassium ferrocyanid is injurious to the fig. *Pinus pinea*, *Pinus sylvestris* and *Ligustrum* appeared to resist its toxicity. Caterpillars on treated pines were unaffected. The toxic effects are believed to be favored, in the fig, by the lactiferæ present.

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(1c-77)

**Elimination of Dyes.**

*E. Couvreur and H. Clément, Compt. rend. Soc. de biol., 85:1025, Paris, Dec. 3, 1921.*

Attempts to color silk by injecting neutral red within the celom of silkworms (*Bombyx mori*), were unsuccessful, but suggested study of the elimination of coloring agents in higher animals, such as dogs and rabbits. Subcutaneous and intravenous injections were employed. In the former method, the stains used were neutral red, eosin and methylene-blue. The greater part of the stains did not extend far from the site of injection, very little reaching the circulation. Intravenously, the same 3 stains and another, tournesol (a blue stain obtained from lichens) were employed. Blood, bile and urine were withdrawn from time to time by means of a cannula in the jugular vein and biliary and vesical fistula. Relatively large doses of the stains were injected. The experiments showed that the stains were actively eliminated by the kidneys, some (eosin and neutral red) being also eliminated by the liver, the lymph system also aiding. Very heavy doses permit more or less general distribution. Some of the stains must be destroyed by structures not yet determined, for they cannot be found in the blood (methylene-blue and neutral red). The kidneys and liver play an im-

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portant part in the elimination. Study is greatly aided by spectroscopic examination and determination of the behavior toward acid and alkaline media. Elimination is rapid; eosin, injected into rabbits, was undiscoverable after twenty-four hours.

(1c—78)

**Vascular and Nervous Reactions Following Peptone Injection Studied with Certain Stains.**

*J. Gautrelet, Compt. rend. Soc. de biol., 85:915, Paris, Nov. 17, 1921.*

The adsorptive property of thionin and other stains is utilized. Although of the same group as methylene-blue, thionin does not affect the heart or blood pressure of the normal dog, even though 1, 2 or 3 cg. per kilo body-weight be injected intravenously. Nigrosin, grouped with indulins produces marked and persistent hypotension in doses of 0.5 to 1 cg. per kilo body-weight. Carotid pressure falls rapidly, 5 to 6 cm. Hg., the original pressure not being regained after three-quarters of an hour. If the nigrosin has been preceded by 1 cg. thionin per kilo body-weight, hypotension is still more marked, falling almost to zero and remaining very low for over an hour. The oncograph registers vasoconstriction corresponding to splanchnic dilatation. Atropin, adrenalin and ergotoxin fail to prevent the hypotension; 1 mg. pilocarpin per kilo body-weight, followed by thionin, prevents the nigrosin pressure-fall, which is thus shown to be due to the thionin-nigrosin combination. Vasomotor parasympathetic paralysis is induced. In a dog injected with 10 cg. Witte's peptone per kilo body-weight twenty-four hours before, the thionin-nigrosin complex produces no cardiac or vascular change. In a dog transfused for one minute from a peptonized donor, the thionin-nigrosin complex also fails to act. Whether a dog is injected with peptone, atropin, or neither, nigrosin alone lowers pressure; but injection of thionin during the period of hypotension restores pressure to the original within five minutes. A substance, circulating in the blood, appears after peptone-injection; this substance counteracts and prevents the hypotensive action of nigrosin; it acts similarly to pilocarpin (parasympathetic stimulant); thionin fixes it by adsorption. The thionin-nigrosin complex is important for studying this.

(1c—79)

**The Action of Ethereal Oils upon the Leukocyte Count in Rabbits, Using Different Methods of Injection.**

*Johannes Burmeister, Berl. klin. Wchnschr., 58:1407, Nov. 28, 1921.*

Ethereal oils, such as the oils of camphor, turpentine, mustard, cinnamon, peppermint, fennel, etc., have been used internally as well as externally. They inhibit the growth of bacteria rather than kill them. In 1917, Klingmüller introduced the subcutaneous injection of turpentine and other oils. The immediate effects of such injection are: fever, local, focal and general reactions, as well as alterations of the blood-picture. The multiplicity of the action indicates a nonspecific stimulation. The author tested the results of parenteral injection of different ethereal oils on the blood-picture of the rabbit and found that subcutaneous, intramuscular and subfascial injection of increasing amounts produced leukocytotic alterations. The strongest effect was produced

by subcutaneous injection; next ranked the intramuscular, and then the subfacial method, while intravenous inoculation produced the weakest effect. Cinnamon oil is strongest in its action; then follow in order: Oleum eucalypti; ol. terebinthinæ; ol. pini pumilionis; pini silvatici; ol. rosmarini. The smaller the surface of resorption, the stronger the leukocytotic action.

Since the effect of these oils varies inversely with the degree of resorption, their therapeutic action cannot depend on a positive chemotactic increase in the number of leukocytes, but is probably due to non-specific physicochemical cell alteration, in the course of which certain decomposition products are formed, which in turn stimulate increased cell activity.

(1c—80)

**Tests with Oils of Cade.**

*R. Huerre, Bull. d. sc. pharmacol., 28:508, Paris, Nov., 1921.*

Codex requirements for oil of cade may be satisfied by pyroligneous oils not derived from Juniperus oxycedrus. Given such an oil, lighter than water, not coloring green by the Hirschsohn-Pépin test and distilling at least 60% between 15° and 300° C., the lighter oils of pine tar are excluded, also oil derived from Juniperus phoenicea, according to Pépin. The given oil is treated with dilute soda and other technic carried through, as follows: 25 c.c. of the oil are placed in a decantation flask with 35 gm. aqueous soda solution (10 gm. soda and 25 gm. water). The mixture should be actively agitated five or six times during an hour; after six hours' rest, the alkaline liquid should be separated and 25 gm. water added. Shake and separate. Treat three or four times with water, until washings are no longer alkaline; at this point, add 25 c.c. ether, dehydrate the ethereal solution by anhydrous sodium sulphate, filter, distil the ether and weigh the residue. Of the latter take 5 gm. and, avoiding elevation of temperature, add gradually to 15 gm. glacial acetic acid saturated with HCl and contained in a flask with ground-glass stopper. Shake and set aside for twelve hours. Whether crystals are then formed or not, transfer the total contents to a crystallizing vessel and leave in the cold. Any crystals resulting should be collected on plain filter paper, dried at laboratory temperature with several thicknesses of filter paper, and weighed. Tests were made with 2 oils of cade prepared by the author, one derived from wood obtained from the department of the Var (1914), the other from wood of the Pyrenees Orientales; on 4 oils guaranteed genuine by the best Paris Pharmacies; on an oil of Lebanon cedar and an oil of Juniperus virginiana; on a veterinary oil not giving the green color of the copper acetate test; on a light oil of pine tar; and on an oil of Cedrus atlantica. Crystals thus obtained consist of levorotatory dichlorhydrate of cadenin; under the conditions of the test, Juniperus oxycedrus alone yields crystals, levorotatory and consisting of cadenin dichlorhydrate, by the action of hydrochloric glacial acetic acid on the portion of a pyroligneous oil lighter than water, insoluble in dilute soda. A table shows insolubilities in dilute NaOH, temperatures of test, temperatures of crystallization and weights of crystals obtained.

(1c—80)

(1c-81)

**The Effect of Sodium Taurocholate on the Surface Tension of Water.**

*E. Doumer, Compt. rend. Soc. de biol., 85:1138, Paris, Dec. 17, 1921.*

Under the action of increasing quantities of sodium taurocholate, the surface tension diminishes in a curve precisely the same as that already established for sodium glycocholate. Both salts thus follow the same law. The power of the taurocholate to lessen surface tension is not so great as that of the glycocholate, for the same quantity of the salt. One and one-half times the quantity are required to produce the same degree of decrease. The salt used for the test was obtained from the dog. To its water solution, 0.1 gm. of soda per liter was added to avoid acidity. The calculated decrease in surface tension closely agrees with that determined. The quantities of taurocholate tested, per liter, were 1, 2, 3, 4, 6, 9, 12 and 15 dg.

(1c-82)

**Action of Sugar on the Heart.**

*Attilio Busacca, Arch. di farmacol. sper., 31:86, 97, 113, 134, Rome, March 15, April 1, 15, May 1, 1921.*

This work concerns the action of various sugars, administered parenterally in various concentrations, upon frogs' hearts *in situ*; 1 c.c. each of the solutions mentioned was used in each case. Sucrose in concentrated solution (100 gm. in 100 c.c. distilled water) caused almost immediately a greater amplitude of the cardiac excursion with a diminution in rate. With onset of fatigue there was a gradual return to normal. Injections of the same sugar in a 1% solution caused an increase in both rate and amplitude per beat. Glucose in 100% solution caused at once an increase in amplitude and a reduction in rate; in the 1% solution, glucose caused an increase in both amplitude and rate. Lactose in saturated solution caused an increase in amplitude with a reduction in rate; in a 1% solution, lactose caused identically similar results: greater amplitude and lessened rate. Observations as to the effect on blood pressure were then made on dogs. Injections of sucrose in saturated solution caused uniformly a rise in pressure, this rise being in direct ratio to the total quantity of sugar injected. In order to determine whether the degree of concentration of the sugar solution played any rôle and, if so, to what extent, exposed frogs' hearts *in situ* were watched while sucrose in various concentrations was injected. The slowing of the heart-rate was then shown to depend not on the concentration of the sugar solution employed, but on the total quantity of sugar injected. In animals watched until death it was shown that the heart rate gradually slowed with the increase in the quantity of sugar injected, an average frog of 20 gm. being killed by the injection of a total of 4 c.c. of a saturated solution of sucrose. In view of its effects, therefore, sugar is now used in various cardiac affections with marked beneficial results. These pharmacologic principles may be enunciated: Small doses of sugar exert a tonic action on the heart muscle, cause an increase in systole, rise in blood pressure, increased heart rate, diuresis and vasodilatation; large doses act as a tonic on cardiac muscle, cause stronger systoles, longer diastoles, lowering of heart-rate, rise in blood pressure and vasoconstriction. The smaller doses are therefore indi-

(1c-81)

(1c-82)

cated in cases of general collapse, heart disease with low pressure, and in angina pectoris. The larger doses find their field of usefulness in all other cases where a general improvement in cardiac action is desired. Lactose may be used for either effect in small doses, eliminating the risk of nausea. On the whole, sugar therapy in cardiac affections precludes the danger of the cumulative effects of the digitalis group of drugs.

(1c—83)

1c—83)

Action of Substances Extracted from the Heart of the Tortoise upon the Frog's Heart.

J. Demoer, *Compt. rend. Soc. de biol.*, 85:1091, Paris, Dec. 10, 1921.

The frog's heart, suitably isolated and arranged for perfusion and plethysmographic record, is irrigated successively with Ringer's solution, with or without glucose, aqueous extract of frog's heart, and serum plus aqueous extract of tortoise heart. The first 2 liquids cause no change in the time relations or force of the contraction from those ordinarily registered. The tortoise heart extract diminishes the force of the cardiac contractions and slows the period. It does not seriously affect the life of the cardiac muscle, and the normal relations of time and contraction strength reappear on withdrawal of the tortoise heart extract. It was found that an extract prepared from the skeletal muscle of the tortoise very seriously affects the frog's heart, often arresting it; such an extract is therefore toxic to the frog's heart. Tortoise heart extract is probably somewhat toxic to the frog's heart and is antagonistic to the normal exciting mechanism, as indicated by the altered rhythm observed.

(1c—84)

(1c—84)

Action of Substances Extracted from the Auricle and Ventricle of the Canine Heart upon the Isolated Rabbit Heart.

J. Demoer, *Compt. rend. Soc. de biol.*, 85:1093, Paris, Dec. 10, 1921.

Various experiments tend to show the existence of active and specific cardiac substances. The author has studied the isolated rabbit's heart, maintained at constant temperature and saturated with oxygen. The liquids tried out upon the heart so prepared were (1) Locke's serum with glucose plus aqueous extract of the dog's cardiac auricle, (2) the same plus aqueous extract of the dog's left ventricle and (3) the same plus aqueous extract of the dog's skeletal muscle. The first solution usually alters the cardiac contractions, either by augmenting the general amplitude or increasing the tonus. The effects seem to be more marked upon the tonus. The rapidity of the beat is increased. The second mixture often weakens the cardiac contractions and slows the beat. It is not toxic to the rabbit heart. In one series of tests, no effect was produced by this mixture. The third liquid is rarely toxic and usually produces little or no effect.

(1c—85)

(1c—85)

Gastric Action of Some Drugs and Endocrine Substances.

F. Durant, *Arch. di farmacol. sper.*, 31:177, Rome, June 15, 1921.

These experiments were performed upon cats' stomachs, removed and emptied of their natural contents immediately upon death of the  
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animal, and immersed in Ringer's solution through which oxygen was slowly bubbling. Enough of the solution within the stomach was removed before the injection of each substance tested to obviate the complication of difference in pressure, and the temperature was maintained at 38° C. throughout, for it was found that chilling increased the tonicity, whereas greater warmth increased the motility of the organ. Atropin caused a lessening of motility and a slight lowering of tonicity; ergotin caused an increase in both motility and tonicity; cascara caused an increase in motility with only a slightly increased tonicity. Pituitary substance caused a slight increase in tonicity but a marked increase in motility; thyroid extract caused both a very markedly increased motility and tonicity; suprarenal substance caused, in less than one minute, an increase in motility; pancreatic extract caused also a prompt increase in tonicity and motility. Adrenal substance, followed in twenty minutes by atropin, caused practically no change, showing that adrenal substance inhibited the depressing effect of atropin; with adrenal substance and cascara, there was an inhibition of the tonic effect of the latter drug. Thyroid was shown to inhibit and modify the depressing effect of atropin and, to a more marked degree, the stimulating effect of cascara. Pancreatic extract also inhibited the depressing effect of atropin as well as the stimulating action of cascara. Pituitary substance attenuated greatly the depressing effect of atropin, but just as greatly enhanced the stimulating action of cascara; pituitary extract also increased the stimulating effect of ergotin.

(1c—86)

**Conduction of Adrenalin along the Nerves.**

*S. Rebello and M. Pereira, Compt. rend. Soc. de biol., 85:1163, Paris, Dec. 17, 1921.*

The results obtained by Lichtwitz, Meltzer and Lépine are reviewed. Lichtwitz's experiments were repeated on *Rana esculenta*. Pupillary reactions were studied by Abbe's light chamber, applied to a dissection hand-lens, magnifying 5 diameters. Results varied between marked cutaneous hypersecretion, total dilatation with rigid pupil, a positive reaction of moderate intensity and absence of any skin or eye reaction. In the cases of pupillary dilatation, there was noticeable exophthalmos. The average period between injection and response was thirty-two minutes. The induced mydriasis resisted local application of eserin. There is no doubt, therefore, that the effects of adrenalin may be transmitted by the nerves but is a question whether adrenalin as such may be transmitted.

(1c—87)

**Transmission of the Effects of Adrenalin.**

*S. Rebello and M. Pereira, Compt. rend. Soc. de biol., 85:1166, Paris, Dec. 17, 1921.*

Pupillary dilatation and cutaneous secretion have been obtained by injections of adrenalin made at a distance and transmitted by means of muscular tissue left as a connecting link. The authors have obtained similar transmission by means of the sciatic nerve (in frog preparations). The reactions were given by Ringer's solution, atropin and eserin, as well as by adrenalin. Positive results were also obtained under ether anesthesia. Using synthetic adrenalin, the authors found

(1c—86)

(1c—87)

that 1 c.c. of a 5:1,000 solution, and 0.1 c.c. of a 10:1,000 solution, gave the same reaction as that produced by 1 c.c. of a 1:1,000 solution. Results were negative with solutions of cocaine, which blocks the nerve and prevents transmission. The authors also worked with a muscle preparation, nerve-transmission being excluded. Here, also, the reactions obtained correspond to those described above for the nerve preparation. It is therefore improbable that adrenalin and other substances pass, as such, along muscle or nerve. In general, the effective factor consists of the volume of liquid injected; but adrenalin has a specific action, independent of the volume. It is probable that a sympathetico-tonic condition is produced in the nerve transmitting the impulse which gives the end-effect. Further studies are in progress.

(1c—88)

(1c—88)

**The Hypotensive Effect of Adrenalin.**

*G. Milian, Paris méd., 11:468, Dec. 10, 1921.*

The writer agrees with the conclusion of an article by Girou on the same subject to the effect that adrenalin has a hypotensive action. He has used it in particular in cases of serous apoplexy in order to reduce the blood pressure. In 1 case, a fall of 4 cm. in the maximal pressure was obtained after one injection, and a further fall of 1 cm. after two further injections.

(1c—89)

1c—89)

**Blood Acetone Bodies after the Injection of Small Amounts of Adrenalin Chlorid.**

*Roger S. Hubbard and Floyd R. Wright, J. Biol. Chem., 49:385, Dec., 1921.*

A series of 7 experiments was run on normal men. Each subject was fed a standard simple breakfast, and an hour afterward received an injection of 0.5 or 1 c.c. solution of adrenalin chlorid (1:1,000 dilution). A sample of blood was taken before the injection was given, and other samples were taken at various intervals after the injection. Each sample was analyzed for acetone from preformed acetone plus aceto-acetic acid and for acetone from B-hydroxybutyric acid by the technic described by the author in the preceding paper. Analysis for sugar was made by the technic described by Benedict (1918), and for the carbon dioxid-combining capacity of the plasma by the method of Van Slyke and Cullen (Van Slyke, 1917; Van Slyke and Cullen, 1917). Changes in the systolic and diastolic blood pressure and the pulse rate were also recorded. These last showed no anomalies, except the expected variations with the larger dose of adrenalin chlorid. From a study of the tabulated results it is observed that 3 of the experiments show a distinct rise of the acetone bodies, with a subsequent return to the values found preceding the injection of the adrenalin. The experiments which showed the most marked variations are the experiments in which the subject received a dose of 1 c.c. of the drug. The authors remark there is no constant relationship in the degree of response of the different acetone bodies, and the results in the cases where a rise is noted do not seem to bear any relationship to the changes in blood sugar nor in the carbon dioxid-combining power of the plasma. The magnitude of the rise observed in some cases and the subsequent return

to normal values indicate, the authors claim, that the changes are real changes in the substances present in the blood, induced by the adrenalin chlorid administered.

(1c-90)

(1c-90)

**Influence of Adrenalin on a Provoked Hypercalcemic Curve.**

*Juan M. Muñoz, Rev. Asoc. méd. argentina, 34:734, Buenos Aires, Sept., 1921. Also Compt. rend. Soc. de biol., 85:954, Paris, Nov. 17, 1921.*

Experiments were made with the injection of a 10% solution of  $\text{CaCl}_2$  in physiologic solution, into the jugular vein of normal dogs, at a ratio of 0.01 gm. calcium per kilo of body weight. This was done to the controls. In addition, the test animals received adrenalin in intravenous injections of 1 c.c. of a solution of 1:200,000. The animals fasted during the experiment. The intravenous injection of calcium in normal dogs caused a rise of the calcium content of the serum, which lasted from three to six hours, and was followed by a fall to subnormal. Intravenous adrenalin injections did not appreciably modify the variations caused by injection of calcium. The rise of calcium in the blood of normal dogs lasted from two to four hours, after which it fell below normal. The influence of adrenalin injections on the hypercalcemic curve can be interpreted as a retention of calcium in the blood in measurable proportions.

(1c-91)

(1c-91)

**Adrenalin Hyperglycemia.**

*Brösamlen, Deutsch. Arch. f. klin. Med., 137:299, Leipzig, Oct. 21, 1921.*

Adrenalin hyperglycemia is not as common in man as in animals. It was observed 4 times in 35 cases examined, once each in connection with exophthalmic goiter, endogenous obesity, tuberculosis and myelogenous leukemia. Injections of adrenalin always produced hyperglycemia. Serial tests were made with Bang's micro-method. Adrenalin Höchst was given subcutaneously in doses of 1 gm. These injections were followed by marked subjective disturbances. In 8 healthy subjects the blood sugar titer was definitely increased twenty minutes after injection; the maximum is reached after an hour, and two to three hours later only slight hyperglycemia persists. Five tests in a case of exophthalmic goiter showed that in this disease the titer rises higher than in normal people. In health it increased 0.5%, in Basedow's disease 0.7%. Blood pressure rises later, and has returned to normal before the hyperglycemia has reached its zenith. Affections of the thyroid gland do not show highly increased blood sugar index after injections of adrenalin, but a marked acceleration of the pulse. A case of myxedema reacted very little, so far as blood sugar was concerned. An adrenalin action was noticed in 8 cases of diabetes. The severity of the disease does not exert any influence on the increase of blood sugar by injections of adrenalin. Diabetes may be attended by a diminished index. If the case is easily influenced by nervous impulses, the blood sugar index rises noticeably.

(1c-92)

**Adrenalin and Alimentary Glycosuria in Experimental Icterus.**

*Alessandro Rossi, Arch. di farmacol. sper., 31:79, 81, Rome, March 1, 1921.*

The author had previously shown that there existed a very marked similarity in the pharmacologic actions of adrenalin and bile, both on isolated organs and *in situ*. Since adrenalin acts as a sympathetic tonic hormone by stimulating the sympathetic nerve endings, experiments were made to determine whether bile acts in a similar manner. According to Langley and von Noorden, the glycogenic function of the liver depends upon the sympathetic (stimulation) and the vagus (inhibition). Any adrenalin injected from the outside enhances the effect of the adrenalin circulating in the blood by a summation of stimuli, and results in a greater glycogenic activity of the liver. If bile really acts like adrenalin, its administration should result in a similar summation. Experiments on rabbits (shown to be particularly sensitive to adrenalin) have almost uniformly shown that the substitution of bile for adrenalin in increasing amounts caused a progressively increasing glycosuria, all other factors being equal. Hence one may assume that bile is a stimulant of the sympathetic nerve endings. Experiments were then made with a view to establishing a similar relationship in alimentary glycosuria. Dogs were used for this work. However, all results were negative, although this species showed the same reaction to adrenalin. A summary of the present state of our knowledge of the subject includes the following principles: In individuals who do not yield a glycosuria following the administration of adrenalin, such glycosuria may be obtained by a preliminary administration of atropin. In some cases, such adrenalin glycosuria may be inhibited by the previous administration of pilocarpin. Neither atropin nor pilocarpin have any effect on alimentary glycosuria. In diabetics, adrenalin causes an increased sugar output; however, no effects are obtained in patients whose urine has been rendered sugar-free. As to clinical icterus, it has been shown that the carbohydrate tolerance is diminished in catarrhal and cholelithic jaundice, but remains unchanged in hemolytic or pernicious anemia jaundice.

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(1c-93)

**Changes in the Distribution of Urinary Nitrogen Produced by Subcutaneous Injection of Adrenalin.**

*J. Brel, Compt. rend. Soc. de biol., 85:1057, Paris, Dec. 10, 1921.*

One milligram adrenalin per kilo body-weight was used, the studies being made in rabbits. Under normal nutrition and diet, urinary nitrogen is increased. The same statement often applies to the resulting ratio of amin to total nitrogen. The quantity of protein nitrogen should be subtracted from the total. The same results may appear in the fasting animal. However, in one test the nitrogen ratio was lowered and a slight amino-aciduria was induced, continuing to the death of the animal. In animals at first deprived of food and then fed, transitory variations in nitrogen occurred. In one test, the ratio fell from 85 to 54, while that of ammonia-nitrogen rose from 0.13 to 0.26, the amino-nitrogen rising from 0.38 to 11.3. In an animal fasting for four days, which had previously reacted as usual, variations similar to those just

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mentioned occurred when the animal was fed on the day following the test. Although these experiments are not final, adrenalin appears to promote urea formation, owing to its stimulation of the hepatic function of splitting amino-acids. Prolonged fasting, or feeding after fasting, appear to produce hepatic insufficiency which is revealed by the injection of adrenalin.

(1c—94)

(1c—94)

**Pharmacodynamic Study of Adrenalone; Site of Its Vasoconstrictive Action and Effects in Presence of Various Vasomotor Drugs.**

*E. Jaeger, Compt. rend. Soc. de biol., 85:910, Paris, Nov. 17, 1921.*

Section of the cord below the medulla was made, after division of the vagi and establishment of artificial respiration (dogs). Intravenous injection of adrenalone produces typical renal vasoconstriction, with marked rise of arterial pressure. The action of adrenalone and adrenalin is identical, except that the effects of the former are more durable; its vasoconstriction is not cerebrobulbar, but peripheral, as shown by its effect on the mucosa, cutaneous bleeding, etc. One drop of a 1:10 solution, injected into the skin of the human forearm, produces a white spot visible for some twenty hours. The site of action is therefore in the peripheral endings of the sympathetic. Adrenalone is antagonistic to vasodilators, the action being strongly shown with histamin. The fact may be applied in quantitative determination of adrenal substances. After ergotinin, adrenalone produces transitory hypotension, the hypertensive effect of ergotinin soon being resumed. Nitroglycerin is not favorable for study with adrenalone, since its effect is tardy and occurs in two stages.

(1c—95)

(1c—95)

**Altered Toxicity of Drugs Injected in a Sugar Vehicle.**

*Attilio Busacca, Arch. di farmacol. sper., 31:69, Rome, March 1, 1921.*

Morphin and cocaine were injected into frogs in both aqueous and sugar solutions (100 gm. sucrose in 100 c.c. distilled water), in various doses, to determine the relative lethal dose. Morphin hydrochlorid was used. Repeated experiments showed that the toxicity of morphin was greatly increased when the drug was injected in a sugar vehicle, as shown by the rapid death of the animals with lethal or slightly sub-lethal doses and more powerful drug action with smaller dosage. This should be of importance in the treatment of morphinism, a sudden massive reduction in the amount of the drug being rendered possible, and should prove of interest to the surgeon for administration of the drug preliminary to general anesthesia. Cocaine hydrochlorid was similarly experimented with, and the results also pointed to an increase in the pharmacologic action and toxicity of the drug when injected in the sugar solution. This will render possible a reduction in the usual amount of cocaine needed for local anesthesia in any case, as well as for spinal anesthesia, for the findings hold for all cocaine derivatives. The results of experiments with phosphorus (glycerin-phosphoric acid), arsenic (sodium cacodylate) and iodin were reported in a previous article.

(1c—96)

**Poisonous Effects of Salts of the Heavy Metals on Vegetable Plasma.**

*Hugo Kahho, Biochem. Ztschr., 122:39, Berlin, Sept. 26, 1921.*

The salts of the heavy metals possess the same valency, though different colloidal activities, and hence unequal toxicity toward plasma. This is related to the degree of electrolytic solution pressure of the divalent cations of the heavy metals. To investigate the connection in regard to vegetable plasma, experiments were conducted with sections of epidermis of red cabbage. Concentrations of the salts of heavy metals of 0.175 mol. and 0.025 mol. at 17°-20° C., were employed. The epidermic sections were placed in these for varying periods and tested for cell death by plasmolysis in sugar solutions. The sequence of the electrolytic solution pressure is: Hg, Cu, Pb, Ni, Co, Fe, Cd, Zn, Mn, Ca. In relation to this the toxicity of the cations, arranged in descending order of toxicity, behaved towards the stronger concentration = Hg>Cu>Zn>Pb>Fe, Co>Mn, Cd, Ni>Ca, and toward the weaker concentration = Hg>Cu, Zn>Pb, Ni>Fe>Cd>Co>Mn>Ca. In the latter case, therefore, the behavior was generally in correspondence with the electrolytic solution pressure. The anions do not seem to play any part herein, but the deviating behavior of some cations points to the possible coexistence of specific influences.

(1c—97)

**The So-Called Saturnine Asthma.**

*Ettore Tedeschi, Riforma med., 37:1117, Naples, Nov. 26, 1921.*

Opinions differ as to whether "saturnine asthma" is of itself a syndrome or is only a symptom. After studying 2 cases of characteristic lead-poisoning in which the respiratory organs were in a state of spasm, Tedeschi concludes that while saturnine asthma is most often merely symptomatic of uremic or cardiorenal conditions of saturnine origin, and is hence to be considered as uremic asthma, there must, nevertheless, be taken into consideration a saturnine asthma, in which the saturnine etiology is absolutely predominant and of maximum or exclusive importance. In such cases (which are rare), we may speak of "saturnine-bronchial asthma." The endocrine theory considers the asthmatic patient as one stricken with endocrine disequilibrium which under certain conditions will cause an asthmatic state. The disturbance of this equilibrium would occur when one or more glands of internal secretion were injured anatomically or functionally. The action of lead certainly alters one of the most important of these glands, viz., the suprarenal capsule. Thus it is entirely possible for asthma to be directly due to lead-poisoning.

(1c—98)

**Magnesium Sulphate Poisoning in Children.**

*Wm. W. Anderson, J. M. A. Georgia, 10:826, Dec., 1921.*

Twins of 11 years, who had had measles and pneumonia at the age of 5, had had difficulty in walking since that time. Both children could waddle about with knees and legs flexed, walking on their toes and swinging their bodies from side to side, resembling a duck. The stools of one showed ova of *Uncinaria americana*, and of the other, ova of *Tenia nana*. Treatment for the intestinal infection consisted of 2 oz.

(1c—98)

saturated magnesium sulphate solution. Following this initial dose each child passed about 4-5 large, loose watery stools. Breakfast was omitted the following morning, and at 6, 8 and 10 a. m., they were given 8 gr. oleoresin of male fern and 8 gr. thymol, respectively. At 12 m. each was given 1 1/2 oz. saturated magnesium sulphate solution. Following the second dose of magnesium sulphate there was no purging. Ten hours following the second dose both children were in a profound state of collapse. They complained of intense abdominal pain, of being hot, of nausea, and vomited coffee-ground vomitus almost continually so that no food or liquid could be retained for forty to forty-eight hours. They would sink into a comatose state with eyes rolled up under half-closed lids, with breathing scarcely perceptible, slow and deep. At all times, however, they could be aroused and their mentalities were clear. The extremities were icy cold, the pulses could not be palpated at the wrists for about twenty hours, and the heart sounds were very weak and rapid. There was no jaundice, no spasms, or convulsions. The abdomens showed slight rigidity, not localized. There was marked suppression of feces and urine for about twenty hours. High irrigations of normal salt solution and proctoclysis of 5% glucose were begun, after which the bowels eventually moved, the vomiting ceased; the children were able to retain a little strong coffee after about forty-eight hours. The pulses became palpable at the wrists, respiration improved and the stuporous condition slowly passed away; within four to five days the children were in the same condition as on admission. The writer concludes that magnesium sulphate taken by mouth may be absorbed into the circulation and cause serious, perhaps fatal, poisoning, particularly under the following conditions: In concentrated doses, in overdoses, in frequent small, concentrated doses when an accumulative action may occur, in debilitated conditions, as perhaps in the 2 cited above, and when not followed by active purging.

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(1c-99)

**A Note on the Blood Chlorids in Mercuric Chlorid Nephrosis.**

*John A. Killian, J. Lab. & Clin. Med., 7:131, Dec., 1921.*

A number of workers have shown that mercuric chlorid poisoning is characterized by marked retention of nitrogen in the blood and diminished output in the urine. But despite the insufficiency of the kidney in elimination of nitrogenous waste there is usually no edema, a circumstance apparently correlated with the fact that the retention of nonprotein nitrogen is not accompanied by increase of blood chlorids. The low concentration of the blood chlorids has been noticed several times and it has been shown that the progress of kidney insufficiency keeps pace with the drop of alkali reserve of the blood and the excretion of ketone bodies. Restoration of the normal acid-base equilibrium of the blood was accompanied by a return to normal in kidney functioning. The author reports the daily findings in two nonfatal cases. Both patients responded to treatment by gastric lavage, daily hot packs, and daily hypodermic injections of 1000 c.c. of 0.7% NaCl solution or Fischer's solution.

(1c-99)

Case	Date 1921	Chlorids	Uric Acid	Urea N	Creat- inin	CO <sub>2</sub>	Combining Power c.c. per. 100
		as NaCl %				..	
1. R. S., female, aged 19, 15 grains HgCl <sub>2</sub> taken	May 9	0.495	..	22	..	36	
	" 11	0.338	8.3	90	10.7	..	
	" 13	0.388	..	88	9.1	30	
	" 15	0.114	..	98	12.0	27	
	" 17	0.207	..	73	12.0	..	
	" 19	0.250	8.0	75	9.3	..	
	" 21	0.363	2.8	91	7.8	81	
	" 27	0.500	1.0	18	4.4	61	
	June 6	0.525	1.9	13	2.2	..	
2. E. F., female, aged 20, 15 grains HgCl <sub>2</sub> taken	May 17	0.382	9.6	146	14.5	36	
	" 23	0.410	10.9	188	15.8	25	
	June 11	0.563	1.5	11	2.2	..	

The studies were made on whole blood. According to Myers and Short, the chlorids of normal whole blood are between 0.45 and 0.52%. Both the author's cases show decrease in blood chlorids, very marked in case I. Similar findings have been reported by McLean for the chlorids of the blood and urine in lobar pneumonia.

(1c—100)

**The Treatment of Acute Phosphorus Poisoning.**

*H. V. Atkinson, J. Lab. & Clin. Med., 7:148, Dec., 1921.*

Three series of dogs were given phosphorus. In the first series 0.5 gm. was administered in cottonseed oil, in castor oil and in liquid petrolatum, respectively. The first and second mixtures caused death, and the dogs given phosphorus in liquid petrolatum exhibited symptoms of poisoning for only three hours, after which they appeared normal. In the second series the dogs received the same dose of phosphorus in carbon disulphid followed an hour later by magnesium sulphate, castor oil, or liquid petrolatum. Only the dogs given liquid petrolatum survived. In the third series the dogs were given 0.5 gm. phosphorus dissolved in cottonseed oil and forty minutes later half of them were given 1 oz. of magnesium sulphate and half were given 50 c.c. of liquid petrolatum. The first of these survived for two days and the second for four and a half days. The liquid petrolatum had prolonged the life of the dogs even when the phosphorus had been given in cottonseed oil, but the oil had obviously facilitated absorption to such a degree that death was only delayed. These results indicate that liquid petrolatum should be used in cases of phosphorus poisoning, in combination with lavage. It may, presumably, also be used to delay the absorption of other poisons from the intestine.

(1c—101)

**Suprarenal Capsules and Morphin Intoxication.**

*J. Lewis, Compt. rend. Soc. de biol., 85:1214, Paris, Dec. 17, 1921.*

Lewis has always been able to stimulate the cerebral cortex of rabbits, seven to twenty hours after total extirpation of the suprarenals. Symptoms of morphin intoxication reported by various authors were probably due to the morphin employed as an anesthetic. Lewis' anesthetic has been ether. The dogs, in which morphin-chloral was used intravenously, did not respond as well as those anesthetized only with ether, and died twelve to fifteen hours after operation. In another series of tests, dogs anesthetized with chloral hydrate died, the control

animals operated on under ether surviving. In another series of 3 dogs, the suprarenals were extirpated under ether; on recovery half an hour after operation, they were given respectively 0.20, 0.25 and 0.20 gm. morphin hydrochlorate per kilo of body weight. They died in eighteen, seven and three hours. It thus appears that even anesthetic doses of morphin may shorten the survival of dogs deprived of their suprarenals.

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**Experimental Toxic Hematoporphyrinuria.**

*Pietro Binda, Arch. di farmacol. sper., 31:184, Rome, June 15, 1921.*

It is known that the prolonged intake of sulphonal, trional or veronal may cause hematoporphyrinuria. It has been proposed to call this condition toxic, in order to distinguish it from a similar condition due to other causes. From previous investigations it became evident that hematoporphyrin, administered even in large doses, is completely metabolized in the body; also that in vitro hematoporphyrin is reduced by various tissues, notably liver and muscle. In a first series of experiments it was attempted to discover whether prolonged administration of sulphonal to healthy animals (rabbits) could produce hematoporphyrinuria. In the course of from fifteen days to four months, from 12.5 to 108 gm. of the drug were introduced directly into the stomach. There were symptoms of poisoning, some of the animals died, but at no time could hematoporphyrin be detected in the urine either chemically or spectroscopically. In a second series of animals hematoporphyrin was injected subcutaneously or intraperitoneally. In none of the animals could hematoporphyrin be detected in the urine. Finally, various organs of the dead animals were placed in contact, in vitro, with solutions of hematoporphyrin. These organs reacted exactly like similar organs of normal animals, reducing the pigment. It may therefore be concluded that, in the rabbit, prolonged administration of sulphonal does not cause hematoporphyrinuria; that animals rendered toxic with sulphonal can still metabolize hematoporphyrin injected from without; that organs of animals dead from chronic sulphonal poisoning are able to reduce hematoporphyrin in vitro. Experiments on dogs, whose digestion is so similar to man's, gave equally negative results. It would seem therefore that the occasional hematoporphyrinuria occurring in man is not due to sulphonal or its derivatives, but rather to some anatomic or physiologic abnormality caused by the disease which drives the patient to seek relief in the hypnotic.

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**The Blood in Tetrachlorethane Poisoning.**

*George Minot and Lawrence W. Smith, Arch. Int. Med., 28:687, Dec. 15, 1921.*

The commercial use of tetrachlorethane occasions the exposure of great numbers of people to its poisonous effects. Data here assembled are from an investigation among the employees of a silk plant, to determine whether the occurrence of poisoning could be foretold by examinations of the blood. If so, then exposure could be regulated accordingly. A second poisoning tends to occur more readily than the first and to be more serious. If a second poisoning occurs within two weeks, or several poisonings occur several months apart, it is wisest for the worker to change his occupation. It was determined that the blood

changes can usually be observed before the clinical symptoms have developed. The blood-picture, however, is not to be relied upon aside from the clinical, which is also here presented more fully than in the literature, 68 persons having been examined. The most important of the blood changes is a progressive increase of large mononuclear cells, often reaching 40%. Other abnormalities are: the appearance of many immature large mononuclears; a slight elevation in the white count; a progressive, but slight anemia; a slight increase in the number of platelets. All persons with such a picture do not necessarily develop clinical symptoms, but a percentage of large mononuclear white cells above 12, being the first sign of reaction to the poison, is a signal for close observation. The symptoms develop in about the following order, over a period of several days or a few weeks: general discontent, nervousness, inability to concentrate, loss of appetite, headache, insomnia, abnormal fatigue, free perspiration, drowsiness, nausea, vomiting, constipation, jaundice, increase of gastric and nervous symptoms, confusion, dizziness, generalized abdominal pain, cholemia associated with severe necrosis of the liver cells, very similar to that in acute yellow atrophy; delirium, coma, death. Mild symptoms are relieved by immediate removal from exposure; severe symptoms may progress a few days after removal. The earlier the removal after definite blood changes and slight symptoms, the shorter the time during which patient must remain away from tetrachlorethane.

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**Pathologic Anatomy of Symmetrical Softening of the Lenticular Nucleus in Carbon Monoxid Poisoning.**

*Heinrich Ruge, Arch. f. Psychiat. u. Nervenkrh., 64:150, Berlin, Oct. 24, 1921.*

The most striking feature of the numerous cases of CO poisoning which have been recorded is the bilateral symmetrical softening of the middle parts of the lenticular nucleus (inner portion of the putamen). The majority of authors deal chiefly with the question of whether the softening is caused by a primary encephalitis, set up by the CO effects and afterward leading to the necrosis or degeneration of the cerebral region in question, or whether the primary transformation is of a vascular nature, leading to ischemia or thrombosis and thus resulting in a secondary softening of the portions supplied by the vessels concerned.

Some authors adopt the former and others the latter explanation; a third one was added by Kolisko in his recent publication concerning this subject, in which he attributed a decisive significance to the mechanical processes of the tissues. The circulation within the affected regions of the lenticular nucleus is probably impaired by unfavorable mechanical conditions of the blood supply, to which must be added the decrease of lateral pressure in the highly enlarged carotid, which assumes a serpentine curvature leading to the displacement of the arterial points of origin, and also the edematous swelling of the brain caused by the vascular paralysis. The unfavorable mechanical conditions of the blood supply in the lenticular nucleus, which govern its peculiar predisposition for such affections, concern the arrangement of the long and short central arteries in question, which pursue a retrograde course, so that the blood, impelled in a forward direction, is constrained to flow back in a very acute angle, in order to continue its course.

On the basis of the pathological, anatomical and histological results  
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of the examination of his 12 cases, which are arranged according to the time elapsed since the poisoning and which exhibit various stages of the transformations, the author arrives at following conclusions: The lesion of the red blood-corpuses by the CO and the metabolic disturbance going hand in hand with it leads first to a lesion of the most sensitive parts of the brain, i. e., the cerebral nerve cells. This lesion of the nervous substance is increased by the pressure exerted on the part of the vessels enlarged in consequence of the paralysis of their muscles caused by the effects of the gas. This leads to a primary necrosis of the cerebral nerve cells. If the action of the poison is of longer duration, an irritative encephalitis is developed, which may manifest itself either by the decay of the nervous elements and the abundant formation of granular cells, or as a regular inflammation with hyperemia, blood-effusions into the surrounding tissues and infiltration. A further injurious influence is exerted by the retardation of circulation in consequence of the extension and dilatation of the vessels, which, under certain conditions, favors thrombus formation, especially in the vessels of the lenticular nucleus.

It is hardly possible to decide off-hand by autopsy which are the primary and which the secondary transformations. But as, generally speaking, the fatty degeneration of the nervous elements is more pronounced than that of the vessels (that of the ganglion cells is visible after twenty-four hours), it may be assumed that the nervous elements are the first to be injured, whereas the hyaline and fatty degeneration and the calcification of the vessels are of a later date, leading in their turn to a further lesion of the ganglion cells, so that, in consequence of the failure of circulation, at first several smaller areas of softening are developed, which afterward become confluent, thus forming one large area. The symmetrical areas of the lenticular nucleus may be observed as early as at the end of two days, and their sharp delimitation against the surrounding tissue on the fourth or fifth day. All microscopic sections exhibit a pronounced hyperemia in the area of softening and the surrounding tissue.

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(1c—105)

**The Treatment of Illuminating-Gas Poisoning with Magnesium Perhydrol.**

*Solomon Kottek, Münch. med. Wchnschr., 68:1396, Oct. 28, 1921.*

The author had occasion to observe a severe and a light case of illuminating-gas poisoning, in which the administration of magnesium-perhydrol (Merck) rendered very good service. In the severe case, after blood-letting and artificial respiration, Kottek administered 1 gm. of the remedy every three hours, so as to provide the body with sufficient oxygen. The result was excellent, the patient recovered rapidly, in spite of the fact that a thorough pulmonary ventilation and the associated natural acquisition of oxygen were most difficult owing to external conditions. In the second case, the symptoms were relieved after the administration of a few tablets.

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**Denatured Alcohol Poisoning after Drinking Iodin.**

*Domenico Cattoli, Gazz. d. osp., 42:1106, Milan, Nov. 20, 1921.*

A young woman had swallowed "half a glassful" (about 20 or  
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30 gm.) of tincture of iodin with suicidal intent. She complained of violent headache; abdominal pains; polyuria, the urine being dark red and containing albumin, blood, methemoglobin and traces of urobilin; she showed a light jaundice. There was gradual improvement and recovery in three weeks. None of the classical symptoms of iodin poisoning were noted, such as burning of the mouth and pharynx, vomiting of stained material, acute gastric pains, small pulse, ringing in the ears, bloody diarrhea. Neither the patient's tuberculous lesion (left apex) nor her six months' pregnancy could account for the jaundice, which could thus only be due to the poison swallowed, the liver, overworked by the gestation, having for a time been put completely out of equilibrium by the toxic agent ingested. Analysis of the alcohol used as a solvent for the iodin showed it to contain: methyl alcohol 1.9 parts, pyridin .25, and benzol .25 to every 100 parts of ethyl alcohol. The patient had thus taken a total of 3 gm. iodin, 5.7 c.c. methyl alcohol, .75 c.c. each pyridin and benzol, and 20-25 c.c. ethyl alcohol. In the absence of distinct signs of iodin poisoning it is obvious that the denatured alcohol is to be held responsible for the symptoms shown, pyridin being a well known poison and benzol a potent cause of methemoglobinuria.

(1c—107)

**Pharmacologic and Chemical Studies on the Roe of the Pike and Barbel (*Barbus Vulgaris*).**

*Francis H. McCrudden, Arch. f. exper. Path. u. Pharmakol., 91:46, Leipzig, Oct. 11, 1921.*

Of the 3 groups of fish-poisoning, i. e., that caused by eating old or rotten fish, or through the bite, stab or cutaneous secretion of the fish, or from partaking of poisonous though fresh fish, only those fish were studied in which the poison was located in the sexual organs. These were the roe of pike and barbel. A description of the symptoms of these toxic conditions is found in the literature, but chemical examinations were made only in the tetrodons.

In order to determine the nature of the toxic substance of pike-roe, test-meals were given to dogs and cats, and chemical tests were made according to the directions of Takehashi, Inoko and Tohare, to determine if a toxic, organic substance similar to that found in tetrodons could be isolated here. Tests for protamin were made according to directions of Schmiedeberg, Alsberg and Kossel. A sodium chlorid compound was prepared and the lethal dosage in animals determined with it. The salt solution was fractionated with bone and diluted acid, and it was attempted to isolate the toxin with lead acetate, ammonium sulphate, mercuric chlorid in acid and alkaline solution, colloidal iron and last, with dialysis. As the toxin is not in the globulin but in the albumin after the dialysis-test, the former was precipitated from the salt-extract of the roe by means of diluting with water and passing carbon dioxid through it. At another time, the extract, liberated from the salt by dialysis, was separated by centrifuging it. Again, the toxic substance was subjected to autolysis and always tested in animal-experiments. The properties of the toxin could thus be defined. It is soluble in distilled water, cannot be dialyzed and is destroyed by saturation with ammonium sulphate, by colloidal iron, and by heating up to 100° C. It is neither protamin nor globulin, but probably an albumin or some substance extremely difficult to separate from albuminoids, and containing 8-17%

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albumin by analysis. The toxic dose proved to be 0.02-0.04 gm. per kilo of body-weight. The substance is not a ferment and is present in fresh eggs. Its action is not influenced by autolytic changes, exposure to light or preservation (keeping). According to these animal-tests, only the extract of pike-roe, when injected into the circulation, has a strong toxic effect. It attacks the center of respiration, causing a rapidly progressing paralysis and collapse, and also death by asphyxiation. Coagulation of blood and hemolysis do not take place.

The roe of the barbel was studied in like manner and the toxin showed the same character as that of the pike. So far as its chemical nature and other properties are concerned, the toxic dose amounted to 0.85-0.98 gm. The percentage of albumin is 13%. Its action is identical with that of the pike-extract, qualitatively, with this exception—sensory paralysis occurs sooner than motor.

Furthermore, the weight, aqueous volume and connective tissue of the ovaries, the quantity of albumin and globulin and their properties, were determined, in both pike and barbel, and then compared with the findings of Walter in the carp. Although the ichthulin of fish-eggs was formerly compared to the globulin of bird-eggs (vitellin) and considered as important for the formation of hemoglobin, on account of the iron and pirrol contained in it, it was possible to establish the fact that in contrast to these, the ichthulin is free from iron, phosphorus and sugar and does not liberate tryptophan, nor does it show Millon's reaction.

The observation of the globulins of various fishes shows that in the globulin of the carp neither iron nor any reducing substance could be found, while the globulin of the pike reacted to Millon's test, while the globulin of the barbel did not. Likewise, pike globulin contains much phosphorus, while only traces were found in the barbel. And third, the albumin contained in the roe is more similar to vitellin than to globulin. Pike albumin contains iron. In the albumin of the barbel more phosphorus is found than in the globulin. Upon splitting up, the globulin of pike and barbel gives off a reducing substance. These results make it appear probable that the vitellin of different birds also have a variable composition.

From the toxicological point of view, the poison of the barbel resembles that of the pike, with the exception that the poison of the pike is stronger. Its action on the central nervous system consists in causing a rapidly progressing paralysis, and especially that of the respiratory center. The sensory paralysis sets in before the motor one, and death comes by suspension of respiration. When the injections were made subcutaneously or intraperitoneally, manifestations of pain were noticed in various test-animals. Therefore it is possible that vomiting and diarrhea may be caused by similar local stimulations in the stomach and intestinal tract.

We must look upon the active substance in pike-roe and barbel-roe as toxic albumins; they are soluble in water, are destroyed by boiling, are differentiated from Fugu-poison but resemble that of eel-blood and snake-poison so far as the symptoms and chemical properties are concerned. After hemolysis, and when the coagulation of the blood has been influenced, snake-poisons act variably. The intensity of the toxicity of the poisons of eels, snakes and fishes shows as an approximate

lethal dosage, 0.02, 0.0077, and 0.02-0.04 gm. for each kilo of body-weight.

Of those groups which are better known pharmacologically, the toxins of pike and barbel show a great resemblance to the sapotoxins, bodies of the conilin group and temulin. A continuation of these studies is intended.

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#### 1d. BACTERIOLOGY AND PARASITOLOGY

(1d—65) (1d—65)

##### Experiments Showing the Importance of Sequence in Biological Research. I.

*L. Karczag, Biochem. Ztschr., 122:43, Berlin, Sept. 26, 1921.*

A sequence rule is propounded, according to which certain natural processes act best, or least, favorably when carried out in a definite sequence. Such processes, therefore, have a sequence optimum and a sequence pessimum. Ferric salts are capable of effecting considerable acceleration in the velocity of oxidation if the sequence in the configuration of the system be altered. Reactions that may occupy several minutes in a system (Dye — HO) — Fe SO, or HO — Fe SO — Dye, take place instantly, as so-called instantaneous reactions, in a system (Dye — Fe SO) — HO.

For the elucidation of this sequence law, a system consisting of the following components, arranged in consecutive sequence, was employed: (Coli-grape sugar broth) — Antiseptic — (grape sugar broth — antiseptic) — Coli. The antiseptics used were toluol and chloroform (0.01, 0.03, 0.05, 0.10 c.c.). The bacteria were derived from twenty-four hour cultures and used in suspensions in 5-6 c.c. saline solution, the mixtures placed in fermenting tubes in the thermostat and the volume of gas read off at different intervals of time.

The experimental results all show clearly that the samples that had been previously treated with these antiseptics showed inhibition of incubation, fermentation and growth in comparison with the samples to which the antiseptic was added subsequently. From the hygienic point of view, therefore, the true disinfecting range of a substance should be determined, not merely by the results of its subsequent addition, but also by the results obtained on reversing the sequence.

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##### The New Method of Obtaining Cultures from Single Bacterial Cells.

*W. W. C. Topley, J. E. Barnard and G. S. Wilson, J. Hyg., 20:221, London, Nov., 1921.*

In all methods of obtaining cultures from single bacterial cells there is great difficulty in obtaining satisfactory conditions for the microscopic observation of the bacillary suspensions employed. The method described gave 33% successful isolation. Various members of the paratyphoid group were mainly used, but the applicability of the method to certain other organisms proved successful. Procedure: Grow for eighteen hours at 23° C. or six hours at 37° C., a culture of the bacterial strain in ordinary nutrient broth. Inoculate a loopful of this broth culture into a melted and cooled tube of 10% gelatin in 1%

peptone-water. Replace in incubator at 37° C. for two hours. Work with young, actively growing cultures containing relatively few bacteria. Make several preparations by placing on a sterile quartz cover-slip a small drop of this gelatin culture, invert on a sterile glass slide. Slide must be of suitable thickness for use with a dark ground condenser. The film, free from air-bubbles, should completely fill the space between the slide and the cover-slip, without any escape beyond the edge of the latter. These preparations are examined and a cell selected which is moved to the center of the field. The cell is identified with a 2/3 objective. A globule of mercury is then carefully manipulated so as to lie with its center over the cell to be protected. The drop should fill half the field. The bacterial cell is observed in the center of the field, below the center of the mercury droplet. By focusing, the mercury passes out of view and disappears, while the rays entering the objective peripherally form an image of the bacterium. This process is carefully repeated with similar preparations and controls run. These preparations are exposed to ultraviolet radiation (one minute exposure, 3 inches distance from source of light). The exposure is made through a tube of about 24 mm. in diameter, to prevent the incidence of very oblique rays. The preparations are now ringed with melted paraffin, care being taken not to melt the gelatin. Incubate at 25° C. over night. Examination next morning with 1/6 objective and 18 ocular shows a single bacterial cell to have multiplied and formed a colony, while any other bacteria in the preparation have failed to divide. From this preparation cultures are made. With a little practice, the entire manipulation concerned with putting up and exposing a series of 6/10 preparations could be carried out within an hour; unprotected controls take only several minutes. As a result of an hour's work, excluding preliminary and final cultures, it is thus possible to make practically certain of obtaining a culture derived from a single bacterial cell, the whole process being controlled at each step under satisfactory optical conditions.

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**The Course of Vital Staining of Bacteria and the Biologic Effect of Staining upon the Organisms.**

*Fr. Reichert, Cntrlbl. f. Bakteriol., etc., 87:118, Jena, Sept. 15, 1921.*

Experiments were made to determine whether vital staining of bacterial cells could be effected without injury to them, and whether such a staining would make it possible to examine the structure of unchanged bacterial cells. The effects of 53 stains were investigated. An agar culture of typhoid or anthrax bacilli is suspended in 2 c.c. of physiologic sodium chlorid solution or bouillon, or a 2.5% solution of dextrose. One to three loops of this suspension are mixed with varying quantities of the staining solution of varied concentrations. Immediately a differentiation between the suspended bacteria and the staining medium is produced, due to a more intensive absorption of the stain by the bacteria. Malachite green, brilliant green and chrysoidin were found to penetrate immediately into typhoid and anthrax bacilli. Gentian violet, fuchsin, methyl violet, Perkins' violet, dahlia blue, pyoctanin and Victoria blue produce immediate staining only of anthrax bacilli. The pictures obtained with the second group of stains, in presence of sodium chlorid or bouillon, are extremely complicated. The stain is precipitated in

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the form of extremely small globules or flakes, the bacteria form into globules as in agglutination, at the same time absorbing the precipitated pigment. These stains color typhoid bacilli only after a certain time, which varies with each stain of the same concentration. First, only part of the bacterial cells absorb the stain, and then the other part is colored. Most of these dyes stain only when applied at a higher temperature. By increasing the temperature immediate absorption can be effected even with typhoid bacilli.

The favorable temperature depends to some extent upon the medium used for suspension. The nature and the character of the suspension certainly influence the dispersion of the staining solution, and this, together with the chemical constitution of the stain, the permeability of the bacteria and the presence of protective colloids, has considerable influence upon the staining of the bacteria. The precipitation of the pigment accompanied by agglutination of the bacteria and absorption of the flakes of stain, also occurs in the absence of electrolytes, though the latter considerably increase the speed of the process.

In connection with these preliminary investigations a number of experiments were made to determine the effects of dyes upon the vital functions of bacteria. It was found that anthrax bacilli are killed by dyes within five minutes. Yeast cells are also sensitive and react to stains like the vegetative forms of anthrax bacilli. Anthrax spores are somewhat more resistant, but their vitality is injured after contact with a staining solution for a short time. It is remarkable that such small quantities of foreign matter in the nutrient medium can prevent the development of stable forms in the case of fully developed bacilli and can cause premature degeneration of the vegetative elements, while they do not prevent the growth of spores. Typhoid bacilli are also killed whenever real staining of the cells occurs. The presence of protective colloids may diminish the poisonous effects of stains. Typhoid bacilli seem to be more resistant than anthrax bacilli. However, some viable organisms are found after the bacteria have been in contact with the staining solution for twenty minutes, provided all the free stain is removed from the solution by adding bone-black.

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**Bacterial Cataphoresis.**

Erich Putter, *Ztschr. f. Immunitätsf. u. exper. Ther.*, 32:538, Jena, Oct. 20, 1921.

Under the influence of a difference in electrical potential, the particles of almost all colloids move to the electrodes, either to the anode or to the cathode. This phenomenon is called cataphoresis. The author discusses bacterial cataphoresis, as the influence of water endosmoses has not been studied heretofore. He chose the microscopic method for determining the electric current and its strength. For this purpose he placed the suspension of bacteria (1 loop of a twenty-four hour agar culture) under a cover slip, avoiding the formation of air bubbles, introduced it into a chamber suited for microscopic examination, and observed the direction of movement the bacteria took under the influence of an electric current.

The application of the electric current must be made so that chemical changes of all liquid at the electrodes are avoided, particularly the formation of acids or alkalies. It is also necessary to take into account

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the influence of the glass walls upon the movements. To satisfy the first requirement he used electrodes to bent glass tubes filled with a 3% agar jelly saturated with potassium chlorid. One end of the tubes was submerged in the liquid to be examined, which rose above the microscopic chamber on both sides by the width of the cover slip, while the other end led into bottles filled with a saturated solution of potassium chlorid. These bottles were connected by a similar potassium chlorid agar siphon with another bottle, containing a 10% solution of copper sulphate. A copper wire was used to introduce the electric current into the copper solution. The current was taken from a 110 volt system. As soon as the line of the current was closed and seemed to be stationary, the measurements were taken. The theoretically correct value is obtained at one-fifth and four-fifths of the depth of the chamber, as at both of these levels the speed remains constant, while the outer levels are under the influence of endosmosis. As a general rule glass and bacteria have an opposite charge to that of water, which is negative in alkaline and weak acid solutions. This charge decreases with the increasing hydrogen-ion concentration, until discharge takes place. In the presence of peptone the charge of the bacteria can be reversed by acids. Trivalent cations reverse the sign even without the presence of peptone. The bacteria investigated included: *Bacterium coli*, *Bacillus typhosus*, *Staphylococcus*, and *Proteus X 10*. All are strongly negative and hardly show any disposition to reverse the sign of their charge, and their discharge can be obtained only in highly concentrated acid solutions. Their behavior is similar to that of collodion. Of the elementary formations of the higher organism only the cell nucleus seems to possess the same electric properties. At the iso-electric point the globulin-like substances are precipitated, and the albumin-like substances in most cases undergo agglutination, as was shown by experiments with *Bacterium coli*. It seems that under certain circumstances there is a concordance between the iso-electric point determined by cataphoresis and the agglutination maximum. Microscopic study of cataphoresis is superior to the macroscopic method in a U-tube, provided the foregoing conditions are observed, as it obviates the influence of water endosmosis.

(1d—69)

**Bacteriologic Examination of Blood Kept in the Fluid State.**  
*Timar Roza, Orvosi hetil., 65:397, Budapest, Nov. 6, 1921.*

Clotted blood encloses the bacteria and gives a lower percentage of positive results than examinations made at once with fluid blood or with blood kept in the fluid state. The blood was kept fluid by a 4% solution of sodium citrate or 2% sodium oxalate which, however, did not affect the contained bacteria. The experiments were made at the same time as those with sodium chlorid solutions: 0.5 c.c. each of the sodium citrate and of the sodium oxalate solutions were added to test-tubes. Each test-tube received 4.5 c.c. blood, in order to obtain the proper concentration. The bacteria reacted in the same way in both solutions. The tests were made with human blood containing *Staphylococcus*, *Streptococcus*, *Pneumococcus*, *Gonococcus* and *Bacillus typhosus*.

*Staphylococcus* developed well three hours after the blood was drawn off and placed in bouillon or agar. A hemolytic colony developed on Schöttmüller's medium (agar). *Streptococcus* reacted in the same way. Good development was seen with *Pneumococcus* from mixed

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blood on ascitic fluid agar or ascitic fluid bouillon. Gonococcus also grew after three hours' standing, if ascitic bouillon was first mixed with the blood and ascitic agar then inoculated with it. The blood of typhoid patients was inoculated into bile after it had stood for three hours, and was then transferred to agar. *Bacillus typhosus* developed. In twenty-four hours after the blood was withdrawn, live gonococci were found which could be cultivated. These were found in blood treated with the citrate and oxalate solutions and contained a few other bacteria as well. The same was true at room temperature after forty-eight hours and even after seventy-two hours. The experiments show that the *Staphylococcus*, *Streptococcus* and *Pneumococcus* keep in better condition in citrated blood than in clotted blood. This is especially true for the first twenty-four hours. *Bacillus typhosus* is an exception as it perishes in either solution and the control tests showed more typhoid bacilli. The smears of the bacteria, from the citrate or oxalate blood, stain very well with Giemsa and may be used to determine the qualitative existence of the bacteria. The bacteria remain alive for three days and the country practitioner may use these solutions to send specimens for examination.

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**A New Method of Making Bacterial Culture Media.**

*Georg Brünhübner and W. Geiger, Deutsch. med. Wochenschr., 47:1379, Berlin, Nov. 17, 1921.*

Having noticed that there was a luxuriant growth of lower types of fungi on fungi which had been standing a long time, the authors boiled several varieties and obtained a dark fluid which resembled bouillon. The growth of bacteria in this fluid was very different from that on bouillon. Low types of fungi were cultivated on Sabouraud's fungus medium, then on Sabouraud's fungus water and then on the fungus water alone. The growth on the two latter was superior to that on the first. Bacteria did not grow so well. The fungus water was then allowed to stand for six weeks when it was resterilized. Nothing was added to it at this time, but the results obtained were surprising. It is possible to condense the culture medium like Liebig's meat extract and it may be transported in this condition.

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**The Comparative Influence of Pure and Commercial Sugars and of Combined and Separate Sterilization on Bacterial Metabolism.**

*C. G. L. Wolf, Brit. J. Exper. Path., 2:266, London, Dec., 1921.*

Small impurities may affect fermentation reaction. Experiments were undertaken to ascertain whether, with some of the more common organisms, a quantitative difference could be made out when pure and commercial sugars were used, and to investigate the sterilization of sugars with medium. "Chemically pure" samples of commercial glucose and lactose were obtained. In preparing the sugars, received from other laboratories and recrystallized for addition to the medium, the following method was employed: A 20% solution of glucose, made up in distilled water, and made faintly acid to Congo-red with HCl, was tubed off in lots of 20 c.c., and sterilized at 120° C. for thirty minutes. The commercial samples were treated similarly. The organisms em-

ployed were *B. coli*, *B. welchii*, *B. murisepticus* and *B. tetani*. A series of flasks was set up so that under identical conditions and with the same quantity of inoculum there were the following media: (1) Basic medium with pure sugar added aseptically. (2) Basic medium sterilized with pure sugar. (3) Basic medium with commercial sugar added aseptically. The 3 flasks were kept at constant temperature in one thermostat. Duplicates of (1) and (2) were fermented in another thermostat kept at the same temperature. Cole and Onslow's tryptic broth diluted 1:3, giving a nitrogen content for the finished medium about 0.3% was used. A series of tables shows the results. The effect of sterilization on the medium and on fermentation with glucose peptone and lactose peptone in the experiments of *B. coli* are described in detail. While minor differences were encountered, these were not sufficient to indicate that the combined sterilization of commercial glucose or lactose would influence a fermentation reaction sufficiently to lead to error. Such errors might result if more sensitive organisms had been employed.

(1d—72)

**Sugar and Indol Production.**

*Ranque and Senez, Compt. rend. Soc. de biol., 85:937, Paris, Nov. 17, 1921.*

Two conclusions have been arrived at by the authors which have not been referred to by Appelmans: (1) a minimum of 4 gm. glucose per liter is required to prevent indol production entirely in peptone cultures, under the conditions of the authors' tests; (2) if a smaller quantity be used, colon bacilli develop in 2 stages. The first corresponds to that occurring in sugar media, with rapid and regular multiplication, gas-formation and absence of indol. The second corresponds to conditions occurring in nonsugar media, with retarded development, peptone-splitting, production of indol and continuance, for a long time, of the vitality of the bacteria. Studies were made with glucose only. The experience of the authors concerning related sugars and poly-alcohols (mannite) is similar to that of Appelmans.

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**The Formation of Indol and Phenol by Bacteria.**

*M. Neisser, Münch. med. Wchnschr., 68:1384, Oct. 28, 1921.*

In general, only the Salkowski nitrite reaction or the Ehrlich benzaldehyde reaction are used to determine the presence of indol. The examinations of Frieber have shown that both of these reactions by no means have the same value. Frieber showed that the indol-acetic acid formation from the mother substance of indol, tryptophan, is a very common property of bacteria. As Salkowski's reaction is positive to indol-acetic acid as well as with indol, it ought to be positive also with all bacteria, which was found to be the actual fact. The Salkowski reaction as an indol reaction ought to be eliminated from bacteriology. Ehrlich's reaction, on the other hand, has been found absolutely reliable, provided its sources of error (disturbance from very large amounts of nitrite, and disappearance on prolonged subcultivation) are taken into consideration.

The formation of indol is one of the most constant biologic characteristics that is known. The ability to form indol cannot be taken away  
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from indol-positive bacteria even by culturing them under the most varied conditions. The group of indol-positive bacteria includes many representatives of the colon and paracolon group, the dysentery group of the pasteurella varieties, and also other individual bacteria such as the  $X_2$  and  $X_{19}$  protein bacilli, and the ozena bacillus of Perez. Successful experiments are being carried on to use the formation of indol as a test for the presence of intestinal bacteria in water.

The phenol-forming colon and paracolon varieties are widely disseminated; they are found in 80% of cases of both healthy and diseased persons and animals. The simultaneous formation of indol and phenol does not occur in the colon and paracolon varieties, but does occur with certain pasteurella varieties or with the ozena bacillus. The property of phenol formation is also a constant biologic property.

(1d-74)

**Regeneration of the Active Principle Present in Autolysis of Bacteria.**

*J. Bordet and M. Ciucă, Compt. rend. Soc. de biol., 85:1095, Paris, Dec. 10, 1921.*

The growth of microorganisms is inhibited by adding to the culture bouillon a trace of lytic liquid or chemical reagents such as acetone, chloroform, etc. If, however, the lytic liquid (not referring to the chemical reagents) be added, in very small quantity, to a bouillon suspension of living *Bacillus coli*, the lytic principle increases during the bacteriolysis. It regenerates itself, so to speak. It does not increase in sterile bouillon, but requires the presence of living organisms. The latter must be nourished and capable of reproduction. The lytic principle has, therefore, the 2 properties of inhibiting bacterial growth and increasing in the presence of bacteria. These 2 properties are not altered by prolonged contact with chloroform. The phenomenon does not appear if the bacteria are suspended in a nonnutritive solution (normal saline) but is readily produced by supplying them with nourishment. Apparently, lysis is preceded by a phase of bacterial reproduction. The greater the quantity of lytic principle, the more irregular and transitory the reproduction. Lysis cannot occur until the bacteria have lived for a certain time. The experiments described refer only to *B. coli*.

(1d-75)

**Comparative Tests of the Disinfecting Value of Cresol Soap and Aqueous Cresol Solutions.**

*Bruno Lange, Ztschr. f. Hyg. u. Infektionskrh., 94:82, Berlin, Oct. 12, 1921.*

Experiments were made to test the influence of soaps upon the disinfecting action of the cresols on cultures of staphylococci. The disinfecting power of cresol is increased by addition of suitable soap: potassium linseed oil soap being found best. The soap itself, in the concentrations used, had no bactericidal powers. The influence of soap can be observed best in cresol solutions of low concentration (0.2-0.4%); it is unimportant whether the soap is dissolved in distilled or ordinary water. The best proportion of cresol to soap is from 1:0.1 to 1:0.2 with distilled water, and from 1:0.5 to 1:2.0 in city water. If the maximum proportions are surpassed, the soap loses its favorable influence and may even exert a reverse influence. Infected cotton,

(1d-75)

batiste and woolen rags were used. The disinfecting solutions were tricresol, tricresol with sodium oleat, cresol, and cresol soap. The experiments did not proceed regularly, and regular gradations in the strength of cresol solutions between 0.5 and 1.5% could not always be tested. In only a few isolated experiments did the addition of soap in weak concentrations improve the effect. Bacteria in a batiste rag were killed much more slowly than the same number of bacteria in suspension. The results with hard woolen rags were particularly unfavorable. Physical properties of the cloth apparently prevent easy penetration, or possibly even change the chemical properties of the disinfectant. The absence of any difference between cresol and cresol soap solutions and infected batiste rags may be explained by the fact that batiste absorbs soap freely from weak solutions (0.2%) and the concentrated soap in the cloth might disturb the favorable proportion between soap and cresol.

(1d-76)

(1d-76)

**Comparative Methods of Estimating the Value of Disinfection Measures.**

*E. Hailer, Deutsch. med. Wchnschr., 47:1384, Berlin, Nov. 17, 1921.*

The author discusses the difficulties in the determination of a normal value or standardization of disinfectants. He describes the methods used in England and America for the determination of the value of a method or substance. The Lancet method consists of a determination of the "carbolic acid coefficient" and the determinations are made after two and a half and thirty minutes of exposure.

The author rejects the Lancet method on account of the small number of bacteria used which decreases the chances of resistant bacteria being encountered, and because of contamination with substances which hinder bacterial growth. He suggests the use of large pieces of thin, cotton batiste, on which large numbers of highly resistant bacteria can be collected. It is possible to remove the bacteria from the batiste after the test is finished. The method simplifies the introduction of the disinfecting agent, the batiste is not attacked by the disinfectant substances and contains no substances which interfere with the development of the bacteria.

Preparations of cresol previously tested as to its carbolic acid coefficient, were applied to the bacterial carriers (sheets). The results show that the principle of the suspension method is not applicable for practical tests of disinfectants. Errors may occur unless all results are subjected to close scrutiny. Results which are free from error may be obtained by the use of cambric for bacterial carriers. Materials made of animal fibers, as wool or silk, appear unsuitable for this test on account of their easy combination with many substances.

(1d-77)

(1d-77)

**The Importance of Nutrient Media Used for After-Culture in Judging the Success of Disinfection.**

*Bruno Lange, Ztschr. f. Hyg. u. Infektionskrh., 94:125, Berlin, Oct. 12, 1921.*

It was necessary to use an optional nutrient medium for after-culture intended for the testing of disinfectants. The author investigated (Sec. 1—Page 309)

gated the influence of nutrient media upon suspended staphylococci subjected to the action of tricresol (0.6%). Certain changes were discovered during the after-culture, showing that the addition of sugar and other nutritive materials to the bouillon enhanced the growth; but as bouillon in itself is a good nutritive medium, the addition of sugar improved it only slightly. The best medium for bacteria injured by cresol was serum bouillon, next placenta bouillon with dextrose, horse-meat bouillon, horse-meat bouillon with sugar and placenta bouillon. Organisms which did not grow in placenta bouillon, grew in serum bouillon, though slowly. In controlling experiments with uninjured bacteria, the best medium was horse-meat bouillon with sugar and serum bouillon, the worst placenta bouillon. In disinfection experiments the capacity of the medium to neutralize traces of disinfectants must also be known. Cresol is partly neutralized by albumin and particularly by serum. The influence of the medium may be of greater importance in experiments with more sensitive organisms than staphylococci (pneumococci and diphtheria bacilli). Choice of the proper nutrient medium is the deciding factor in judging the influence of disinfectants upon anthrax spores. While a 25% solution of sagrotan does not kill anthrax spores even after fourteen days, in bouillon they fail to grow after treatment with 25% sagrotan for twenty minutes. Dextrose agar plates proved the best medium for anthrax bacilli.

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(1d—78)

(1d—78)

**Chemically Increased Virulence of Apathogenic Bacteria.**

*Bruno Lange and M. Yoshioka, Deutsch. med. Wchnschr., 47:1322, Berlin, Nov. 3, 1921.*

The authors obtained results differing from those of Much, who transformed apathogenic into pathogenic bacteria through simultaneous intraperitoneal or subcutaneous injections of lactic and formic acids. In the first place, Lange and Yoshioka emphasize that the 0.2 c.c. used by Much of a solution up to 1% approaches the fatal dose of lactic acid for the mouse; 0.5 c.c. lactic acid in 1% solution always kills mice; 0.2 c.c. does not. They also dispute the apathogenesis of the bacteria employed. In control tests with destroyed bacteria plus a practically non-fatal dose of lactic acid solution, a few mice died, yet in this instance, we hardly have an instance of "increased virulence." Only partially positive results were obtained in rendering proteus more virulent by cultivating it in nutrient medium of lactic acid.

The authors reached the following conclusions: (1) They failed to render apathogenic germs (air sarcines and hay bacilli) more virulent through added lactic acid inoculation; (2) The effect of inoculation with active and dead proteus may be increased by the simultaneous administration of acid, provided the amount of acid given is large enough almost to equal the fatal dose; (3) this phenomenon cannot be explained, as Much supposes, by "the artificial virulence in connection with the active bacilli." It appears more probable that we have before us the summation of two injuries, per se insufficient to kill the animals (injury to prophylactic power); (4) increases in virulence from the addition of lactic acid to the nutrient medium do not at all exceed present results.

(1d—79)

**Mutations of Bacteria in Connection with Individuality in Bacterial Fission.**

*J. J. van Loghem, Nedrl. Tijdschr. v. Geneesk., 65:2981, Haarlem, Dec. 17, 1921.*

It is usual to apply to the changes which bacteria undergo during their development, notions taken from the theory of heredity and variability in higher organisms. This application is not always possible, however, because of the different value given to the notion of "individual" in bacteria and in multicellular beings. The notion of "individual," however, is fundamental to the notions of heredity and variability. When we speak of heredity, we have reference to a similarity between offspring and parent; if we speak of variability we have reference to differences between them and we consequently presuppose that parent and offspring are different individuals. But this is not the case in bacteriology. In multicellular beings, the descendant is somatically another being; in unicellular beings which propagate by fission, the offspring is not a separate distinct being, but a part of the parent which continues to live as offspring. It may, therefore, be stated that bacterial fission may be characterized as the continuity of the individual. Still, mutations in the character of bacteria take place and the author thinks that these changes depend, either upon the capacity of the bacteria to change themselves, as an individual, so to say, innate quality; or the change may be caused independently of the bacterium and result in a modified individuality; in either case, the modification may involve a gain or a loss. Furthermore, the modification may be permanent or temporary. Consequently, the mutation occurring in the case of bacteria may be studied from the following 4 points of view: (1) The mutation appears as a permanent loss of characteristics. (2) The mutation appears as a temporary loss of characteristics. (3) The mutation appears as a temporary acquisition of characteristics. (4) The mutation appears as a permanent acquisition of characteristics. When studying the character of the mutations here described, we observe that they, phylogenetically, have a regressive character, a kind of atavism, due to the fact that certain tendencies, forming a part of the individual resulting from the fission of the parent-individual, only came to development under certain favorable conditions to which the bacterium adapted itself.

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(1d—80)

**Notes on the Genus Nicolaierillus (Bacillus Tetani). Studies on Pathogenic Anaerobes. VII.**

*Hilda Hempel Heller, J. Infect. Dis., 30:18, Jan., 1922.*

Heller describes certain differences which have been noted in tetanus strains. It is, however, premature to apply these differences to specific differentiation. On complex protein substrates, tetanus strains show remarkable powers of mutation, which are easily observed in colony formation, but do not affect grossly the picture of proteolytic action on meat medium. The morphologic and staining reactions of the bacilli are very characteristic. The behavior of pure cultures on meat medium is fairly characteristic, and is different from that of most common contaminating anaerobes. Meat medium is probably the best protein medium for the differentiation of tetanus strains from other (Sec. 1—Page 311)

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anaerobic organisms. All strains observed were noticeably proteolytic, and none were intensely so. Strains which form large colonies are easily isolated by deep colony procedure.

(1d—81)

**Mutations in the Genus Nicolaierillus (Bacillus Tetani).**

**Studies on Pathogenic Anaerobes. VIII.**

*Hilda Hempl Heller, J. Infect. Dis., 30:33, Jan., 1922.*

Tetanus organisms furnish an excellent field for close study of bacterial mutation, and Heller reports a few such observations in this paper. In protein mediums, in which tetanus strains multiply actively, they mutate readily and much more frequently than do nonproteolytic anaerobes. Some strains mutate more readily than others. The mutations, however, result only in the formation of typical tetanus bacilli; they may be favorable or unfavorable to the existence of the organism. The study of mutating colonies in special mediums makes it possible to determine what metabolic characters are least constant. Mutations are important to both the biochemist and the therapist. Virulence depends very much upon the ability of the organism to multiply in its environment. The colony mutations have no apparent effect on toxin production, although it may be assumed that a strain multiplying extensively will produce a stronger toxin.

(1d—82)

**The Study of Colony Formation in Deep Agar. Studies on Pathogenic Anaerobes. VI.**

*Hilda Hempl Heller, J. Infect. Dis., 30:1, Jan., 1922.*

The members of a pure strain of anaerobic bacteria under uniform conditions form deep colonies differing only slightly from one another. Heller has found, however, that a collection of anaerobic bacilli, corresponding in all ordinary cultural characteristics, may be broken up into groups of strains on the basis of colony formation in deep agar. In some genera, when the medium employed is simple, these groups may be termed "species," but not in others. The observation of colonies may thus be of great value in classification.

The shape of a colony in an agar medium depends primarily on the reproductive power of the organism and on its motility in that medium. The reproductive power depends on the enzymes and metabolic activities. Any mutation involving the metabolic activities of an organism on a given medium may demonstrate its occurrence by causing a change in the colony morphology of the mutating organisms in the strain. Colony formation in deep agar is, then, a phenomenon whose study will be most closely observed by the student of mutation. The colony shape must thus be thought of as a chemical character as well as a morphologic one. The possibilities of its exploitation on specially prepared mediums to test the nature of mutations are infinite.

(1d—83)

**The Pathogenicity of Bacillus Botulinus.**

*Paul F. Orr, J. Infect. Dis., 30:118, Jan., 1922.*

In studying the pathogenicity of *B. botulinus*, Orr found that the optimum temperature for growth and elaboration of the toxin of the  
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organism is that of the body ( $37^{\circ}$  C.). *B. botulinus* was recovered from the internal organs of animals which had been fed or injected with toxic cultures and also with toxin-free spores of the organism. Under certain conditions *B. botulinus* will grow and produce toxin in the body of the guinea-pig. Experimental botulism can be produced in laboratory animals by the feeding or injection of massive quantities of toxin-free spores of *B. botulinus*. The presence of toxin produced in the body as a result of growth in the body, of toxin-free spores, can be demonstrated by the precipitin test as well as by direct toxicity tests. Botulism poisoning in man, due to the ingestion of spores, is probably very rare, if it occurs at all. The possibility of such occurrence must, however, be considered.

(1d—84)

(1d—84)

**Antagonism between *Bacillus Diphtheriae* and *Pneumobacillus*.**

*G. Papacostas and J. Gaté, Compt. rend. Soc. de biol., 85:1038, Paris, Dec. 3, 1921.*

It has been previously remarked that cultures of pneumobacilli impede development of diphtheria bacilli in the same culture. Experiments were made to illuminate the nature of this antagonism. Cultures and injections into guinea-pigs show that the pneumobacillary toxin does not act simply by neutralizing the toxin of the diphtheria bacillus, either in vivo or in vitro. It does retard the growth of the diphtheria bacillus and prevents the usual, abundant production of diphtheria toxin. The pneumobacillus also somewhat modifies the alkalinity of the culture medium. It is not argued that results of these experiments hold good for man, but possibly they explain the benignity of anginas in which pneumobacilli and diphtheria bacilli are associated.

(1d—85)

(1d—85)

**A Superior Method of Isolating the Pneumococcus from the Sputum and the Enterococcus from the Feces, and the Characteristics Differentiating the Two Organisms.**

*N. Pane, Riforma med., 37:1147, Naples, Dec. 3, 1921.*

The feces to be examined were placed on small glass slides in an incubator at  $37\text{--}38^{\circ}$  C. From the third to the twentieth day a slide was taken daily and inoculated into broth culture. The Gram positive Diplococcus intestinalis, or Enterococcus, resists desiccation at this temperature for twenty days, while the other bacteria are gradually destroyed in a few days. In examination of the feces of 40 healthy persons, pure cultures were to be found after the fifth day in all but 3, and in the latter these organisms formed the maximum part, the minimum being a bacillus of the subtilis group. To isolate the enterococcus from this, broth was used containing 1% glucose. The enterococcus then developed rapidly, giving place to acid fermentation, which inhibited the development of the eventual spores of *B. subtilis* or similar forms that might be in the feces. The same method has lately been used to isolate Diplococcus pneumoniae in sputum. In experiments on 30 healthy persons the vitality of this organism was found to be ten days. Streptococci persisted almost as long; from these he isolated pneumococci by means of cultures on nutrient agar. The conclusion is reached that glucosated broth at 1% constitutes the best medium for these desiccated

organisms, whose rapid acid fermentation hinders development even of the sporiferous bacteria present. The most decisive differential characteristic between Enterococcus and Pneumococcus is given by their diverse resistance to desiccation at 37° C., the former resisting twice as long. Enterococcus is larger and always oval; the presence of the capsule in Pneumococcus is always noticeable. If account is taken of the possibility of myriads of pneumococci reaching the intestine from the mouth, and of the fact that in certain intestinal infections the enterococcus becomes pathologic, it cannot be denied that possibly the 2 organisms originally were of the same species.

(1d—86)

(1d—86)

**Occurrence of Virulent Anthrax Bacilli in Cheap Shaving Brushes.**

*Douglas Symmers and D. W. Cady, J.A.M.A., 77:2120, Dec. 31, 1921.*

From 1915 to 1921, 36 cases of cutaneous anthrax were admitted to Bellevue Hospital; in 10, or approximately 28%, the disease followed the use of shaving brushes. During one year and nine months ending October 1, 1920, 34 cases were reported to the New York Department of Health; 17, or 50%, were traceable to shaving brushes. These figures would show that shaving brushes are carriers of anthrax in a large percentage of cases.

Recently a patient was admitted to Bellevue Hospital with a brownish eschar on his chin which was suspicious of anthrax, and was said to have followed the use of a new shaving brush eight days previously. Smears from the pustule revealed innumerable Gram-positive staphylococci, and *Staphylococcus aureus* was isolated in pure culture. Inoculation of a guinea-pig caused its death in forty-two hours. Necropsy revealed changes characteristic of anthrax bacillus, and anthrax bacilli were stained in smears and grown in pure culture.

Following this experience, a series of 40 shaving brushes were purchased from peddlers and in the open market of New York City. From the examination of these, the following conclusions were drawn: (1) In 3 out of 41 instances, or 7.3%, virulent bacilli were found. (2) In 78% of 41 brushes examined bacteriologically, anthracoid bacilli were found, that is, microorganisms presenting much the same morphologic and cultural characteristics as anthrax bacilli but which, when injected into guinea-pigs, are noninfective. The ubiquitous hay bacillus is, perhaps, the most vexatious member of this group. In the bacteriologic investigation of hair and other substances supposed to contain anthrax bacilli, it follows that the infectivity of all suspicious microorganisms should be determined by animal inoculation.

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**Fevers and Febriculas from the Bacillus Asiaticus.**

*Igino Iacono, Riforma med., 37:1165, Naples, Dec. 10, 1921.*

This organism, which was isolated by Castellani in Ceylon in 1905, from the blood and feces, is unknown in Italy, perhaps because it is not customary to make a rigorous search for the etiologic agent in every febrile attack, which it is easier to denominate by a generic term such as intestinal or autotoxic. It produces a moderate fever lasting a few days, without eruption, diarrhea, or liver or spleen symptoms, but

accompanied by wandering abdominal pains of greater or less intensity, yielding to no kind of treatment. Castellani has elaborated a vaccine with which he has obtained good results. The blood serum of these patients does not agglutinate unless there is a mixed infection with that of paratyphoid A or B. From experiments of his own, the author concludes that *Bacillus asiaticus* differs from *B. typhosus* by its immobility and the production of gas from glucose and other sugars; from that of paratyphoid A and B by production of gas in glycerin and by slow development; from the colon and paracolon bacilli by not coagulating milk and by not modifying lactose broth; from proteins and the cloaca group by not liquefying gelatin and serum; from *B. dysenteriae* by production of gas from certain sugars; from *Bacillus entericus* because it does not ferment lactose; and from the alkaligenes group because it does not strongly alkalinize culture media. Hence it belongs in the salmonella group near the paratyphoids and *Bacillus columbensis*, from which it is differentiated by its immobility, by giving off gas in saccharose and by not fermenting dulcin. Its close relation to the typhoid group suggests the need of investigating whether it is not the etiologic agent in cases of fevers and febriculas.

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(1d—88)

***Bacillus Crassus.***

*B. Lipschütz, Med. Klin., 17:1307, Berlin, Oct. 27, 1921.*

The name, "Bacillus crassus," which Lipschütz has given to bacilli found in the purulent secretion in acute ulcer of the vulva is more fitting than names such as Döderlein's "vaginal bacillus" or "Bacillus vaginæ." The former does not correspond to the scientific rules of nomenclature and the latter is impossible because the bacilli are found not only in the original location but also in the cervix and secretion of the urethra, as demonstrated by morphologic and cultural characteristics. The author considers that his method of cultivation of the organisms with secretion from acute vulvar ulcer is of value, since with it it is possible to make a pure culture in his serum agar in forty-eight hours under aërobic conditions.

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(1d—89)

**Note on the Differential Staining of the Granules in Diphtheria and Other Bacilli.**

*Albert G. Nicholls, J. Lab. & Clin. Med., 7:180, Dec., 1921.*

By accident the writer discovered a procedure which brought out very clearly the granules of diphtheria bacilli. The films, fixed by heat, are stained with Neisser's staining fluid No. 1 (methylene-blue, 1 gm.; 96% alcohol, 20 c.c. glacial acetic acid, 50 c.c. distilled water, 950 c.c.). This mixture is allowed to remain on the films for thirty seconds, then washed in water. Gram's iodin solution is applied for ninety seconds, followed by washing in water. Watery solution of saffranin T 0.5% is applied for thirty seconds. The granules appear black on a pink background. The picture is sharp, the contrast excellent. The method is applicable to any bacteria which contain granules, and shows up the granules in diphtheria bacilli exceptionally well.

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(1d—89)

International Medical and Surgical Survey

(1d—90)

**The Interrelationships between the Various Members of the Bacillus Enteritidis-B. Paratyphosus B Group of Bacteria.**

*W. W. C. Topley, H. B. Weir and G. S. Wilson, J. Hyg., 20:227, London, Nov., 1921.*

The purpose of the series of investigations on the epidemic spread of bacteria infection was to gain some knowledge of those biologic laws which must govern the spread of epidemic disease. These past investigations have given rise to the interrelationship of various bacterial groups. The data regarding epidemics of disease, caused by a bacterial species which shows subgroups separate from one another by serological reactions, demonstrates that representatives of all or many of these subgroups take part in the essential progress on which the epidemic depends. In small outbreaks it is a common experience for all clinical cases of the disease in question to be referable to infection by organisms belonging to the same serological subgroups, but in larger outbreaks this uniformity is usually absent.

The writers worked with over 2,000 mice which died as a result of the infection with *B. gaertner* and *B. suispestifer*. The results of their experiments, which are described at length in the text, indicate that the serological distinction between *B. gaertner*, *B. aertrycke* and *B. suispestifer* is less sharp than has been generally supposed, so far as direct agglutination tests are concerned. An organism of one type may acquire the property of being agglutinated to titer by one or both of the heterologous serums. It may become inagglutinable by its specific antiserum at the same time as it acquires the property of agglutinability by a serum specific against one of the other types, a less common occurrence. While this interrelationship is clearly shown by direct agglutination, the same procedure, repeated on many successive subcultures, always reveal the true nature of the strain and the indication so obtained is confirmed by absorption tests. By the experiments the writers found that the serological types dealt with were not bacterial mutants.

The subgroups of the paratyphoid-enteritidis group are briefly recorded, and the sugar fermentation and serological characters are given in each case. A similar relationship seems to exist between *B. enteritidis* and many members of the *B. paratyphosus B* group of bacteria as is maintained between the serological subgroups of such bacterial species as the meningococcus or the pneumococcus. For purposes of classification and nomenclature, *B. enteritidis* should be included within the group and because of priority and of suitability, its name be applied to the whole group.

(1d—91)

**On the Non-Lactose-Fermenting Bacilli in the Stools of Healthy and Unhealthy Uganda Natives. (Preliminary Observations).**

*H. Lyndhurst Duke, Lancet, 2:1212, London, Dec. 10, 1921.*

The stools of 38 normal natives were examined, samples being taken on three successive days in the majority of cases. Specimens were examined as fresh as possible—usually within one or two hours after passage. By "normal" was meant a healthy individual, or a hospital patient suffering from mild venereal disease or from some minor ailment. Stools from 26 natives suffering from typhoid or dysenteric

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disease were similarly dealt with. Stools from 12 abnormal Europeans, all of whom were suffering from some kind of intestinal disturbance, were also examined, and one Indian stool from a case of typhoid. Details of technic are given, with indol tested for by the ether-extraction method, motility investigated in hanging-drop preparations, gelatin employed, lead acetate agar, etc. The various organisms studied were assigned to 10 groups, and the relative frequency with which each of these groups occurred is shown in a table. Group I, for instance, was found in 2 abnormal natives, 10 normal natives, and 2 abnormal Europeans. Rabbits were prepared against 3 strains of organisms of this group, viz., 232e, 234g and 247c, and the other strains were tested against these 3 agglutinating serums. Serum 232e gave complete agglutination at 1/500 with strains isolated from 6 different natives, and gave complete agglutination at 1/40 with a strain from a seventh individual, the 1/500 dilution with this last strain proving negative. With group I strains from 8 other natives, normal and abnormal, no agglutination resulted at either dilution. Serum 234g gave complete agglutination at 1/40, nil at 1/500, with a strain from a normal native. With 14 other strains from group I, isolated from different natives, normal and abnormal, no agglutination occurred at either dilution. Serum 247c gave complete agglutination at 1/500, with strains from 4 different normal natives. With 8 other strains from 4 different normal natives, no agglutination occurred at either dilution. It was plain that at least 2 distinct serological races are included in group I, which is of fairly frequent occurrence in normal natives' stools in Uganda. The recovery on two occasions of organisms of group II from the blood of patients suffering from typhoid-like disease, but whose serums give no agglutination with typhoid or paratyphoid bacilli, indicates that organisms of the *Bacillus foecalis alkaligenes* type may play an important part in the production of enteric disease in Uganda. In the event of a prophylactic enteric vaccine being called for, this type of organism must be considered. The existence within group II of races showing no serological relation to one another must also be borne in mind.

(1d—92)

**The Fluorescens Group.**

*C. Laetzs, Cntrlbl. f. Bakteriol., etc., 87:81, Jena, Oct. 15, 1921.*

Twenty-two strains of *Bacillus fluorescens*, obtained in the course of bacteriologic soil examinations, were examined. They came from all kinds of soil: partly from garden mold, partly from mountain mold, dung water, horse dung, swamp soil, lime rock. The soils were partly collected upon plains and partly upon different altitudes up to 2,900 meters. Three of the strains examined came from the Hygienic Institute of Munich. All of these strains, when examined in a hanging drop, were found to be motile. Suitable staining establishes their partly monotrichic and partly lophotrichic flagellation. A certain number of the organisms are small, straight, slender rods, but some are curved, and frequently one or even several spirals can be distinguished. All have one common characteristic: they do not ferment starch, levulose and mannit. All produce bacteriofluorescin in the cold. The fluorescens strains are very sensitive to heat. The pyocyaneus strains tolerate changes in temperature and also produce another pigment, pyocyanin. But the pigment production varies considerably, even within the same

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strain, being influenced by many conditions little known as yet. Some pyocyanus strains produce only small amounts of pigment, others none at all. On the other hand, the fluorescens strains can be developed to tolerate higher temperatures, thus establishing an uninterrupted link between the 2 groups. The chemical properties also indicate a continuous transition from one group to the other, so far as the power to disintegrate nitrates and liquify gelatin is concerned. Efforts were made to obtain agglutination serum from frogs for purposes of serologic differentiation of the strains. These experiments did not give the desired results.

(1d—93)

**Importance of Amino-Acids in Hemoglobin for the Preparation of Influenza Bacillus Cultures.**

*M. Jakoby and K. Frankenthal, Biochem. Ztschr., 122:100, Berlin, Sept. 26, 1921.*

The study of vitamins has led to recognition of the fact that the food must contain not only the chief ingredients of caloric value, but certain other substances essential to cell components endowed with special functions.

Bacteria lend themselves to studies of vitamins because experiments give rapid results and simplify the methods of research. The influenza bacillus grows only on nutrient media containing blood. In this respect hemoglobin was found especially effective, whereas no growth could be achieved on serum media. Of amino-acids, hemoglobin contains histidin (10.96%) and leucin (up to 30%).

Attempts to obtain cultures of influenza bacillus in hematin media alone, as well as in those containing globin, gave negative results, nutrient media with leucin (1-2 c.c. of 3% solution in 10 c.c. agar) yielded excellent growth. This was also the case when histidin was employed, as well as with a mixture of histidin and leucin in the proportion 1:3, i. e., in the approximate quantities found in hemoglobin. It appears that hemoglobin may be replaced by the amino-acids that occur primarily in its albuminoid component, these results lead to certain conclusions in regard to vitamins.

(1d—94)

**The Influenza Bacillus of Pfeiffer; Its Nutrition and Its Relation to Respiratory Infection.**

*David J. Davis, Illinois M. J., 40:448, Dec., 1921.*

The author's study of this organism has been along 2 lines: first, a study of its nutrition, and second, a study of its distribution and relation to respiratory infections. Its most interesting characteristic is its need of blood or hemoglobin for growth. This blood or hemoglobin medium may be heated for a short time, but the organism will not grow after prolonged heating or autoclave treatment; the heated medium may be reactivated, however, by adding certain animal fluids or plant extracts, thus replacing a second necessary substance. This substance is thermolabile, filterable, resistant to acids but not to alkalis, having in general properties like the vitamins. It seems to control the metabolism of the iron of the hemoglobin in its oxidation activity. This is comparable to the probable control of phosphorus metabolism by fat soluble vitamin A in rickets. Such nutritive need may explain the

symbiosis of the influenza bacillus, whose growth is stimulated by most other organisms grown with it (but not by other strains of influenza bacilli). The different strains of the influenza bacillus belong to a more or less heterogeneous group; there are probably no separate epidemic strains. In distribution the bacillus is confined to the human body, not being found in any animals examined by the author. It is present in normal throats up to 40%, and is found in various diseases. It may cause endocarditis, pericarditis, pleuritis, arthritis and other infectious diseases; experimentally a typical clinical picture has not been produced, so that it has not been proven that it is the cause of epidemic influenza, where it may well be only a secondary invader.

(1d—95)

(1d—95)

**Changes of Streptococci within the Animal Body.**

*R. Schmitzer and F. Munter, Ztschr. f. Hyg. u. Infektionskrh., 94:107, Berlin, Oct. 12, 1921.*

In a previous communication the authors showed that streptococci of low or moderate virulence, after a short passage within the body of mice, lose their hemolytic properties and their virulence is decreased. The present article deals with the effects upon highly virulent streptococci of a short period within the body of mice. By intraperitoneal injection into white mice of a lethal dose, it was possible to cultivate a green species from the peritoneum, heart-blood and kidney within three hours; sometimes pure cultures were obtained if the samples were taken within an hour after vaccination, later more hemolytic colonies were found, and after four or five and one-half hours the strains are exclusively hemolytic. Both species were cultivated for three months on blood agar and serum bouillon without undergoing any change. In 7 of 8 cases the passage of the highly virulent hemolytic species through the body of mice produced mutation into the green variety. These green descendants showed an extraordinary decrease in virulence, or even complete absence of pathogenicity for mice. But under certain conditions the green species reverted again to the hemolytic variety by another passage through the animal body and regained their virulence for mice. The decrease in virulence is not necessarily caused by the mutation, though usually it keeps pace with it. Hemolytic strains, germs after a short passage through mice, could also be cultivated. Their virulence was considerably decreased, while the original species invariably retained its high virulence when cultured on artificial media.

Previous experiments with streptococci of low virulence, were confirmed in these experiments with highly virulent species, i. e., that the green strains do not die within the body of mice, and the remaining hemolytic germs determine the course of infection and cause the fatal outcome. The observation that the mutation and the decrease in virulence in a fatally infected mouse is completed within four hours, constitutes a new phase in the course of infection. This seems to be a transitory immunization, which first leads to a decrease in virulence of the inoculated organisms. Streptococci isolated from the animal body at this stage retain their acquired properties when cultured on artificial media. Within the animal body this phase soon ends and the attenuated green strains regain their original virulence and the infection proceeds to a fatal issue.

(1d—96)

(1d—96)

**Study on the Classification of Streptococci.**

*Etta Fisk and Earl L. Burky, J. Infect. Dis., 30:128, Jan., 1922.*

This study was made for the purpose of classifying streptococci by the appearance of deep colonies in blood agar plates of uniform composition and thickness, by fermentation reactions in various sugars, and by agglutination reactions in the serum of immunized animals. The attempt was also made to show the relationship of the serologic groups to the blood agar and sugar reaction groups. The authors found that the green and the hemolytic types of streptococci are distinct culturally and serologically, the agglutination reactions being used as a measure of the serologic differences. The sugar reactions are not indicators of serologic groupings, but possibly inulin fermentation and the reaction in milk may be of value in group determination in conjunction with the blood type.

(1d—97)

(1d—97)

**A Study of Streptococci from Postgonorrhreal Prostatitis by a Quantitative Method of Agglutination and Absorption.**

*Russell D. Herrold, J. Infect. Dis., 30:80, Jan., 1922.*

The immunologic classification of streptococci and the determination of the relation of these organisms to various diseases have excited a good deal of interest. Herrold studied 28 strains of streptococci from chronic postgonorrhreal infections of the prostate, 4 strains of streptococci from the normal urethra, and 16 from various sources outside the genito-urinary tract. Agglutination and absorption tests were made. Homogeneous emulsions of streptococci were obtained uniformly from young growths on ascites phosphate agar plates. The quantitative method of making suspensions of centrifugated packed bacteria was found to be more satisfactory than other methods of computation, such as counting or comparison with standard barium sulphate suspensions. Two-thirds of the streptococci isolated from chronic prostatic infections were classified by agglutination into 2 related groups. This specificity, however, seems to be limited to the viridans (alpha and alpha prime) types of streptococci.

(1d—98)

(1d—98)

**Cultivation of Tuberle Bacilli.**

*E. Louis Goodman and Mary Moore, J. Infect. Dis., 30:58, Jan., 1922.*

The growth of tubercle bacilli in tubes which had been capped with tin-foil was compared with that in uncapped tubes, as it was thought that the capping might prevent ready access of air to the cultures and that carbon dioxid might be formed in the tube in sufficient quantity to account for the negative cultures in some observations. It was found that human tubercle bacilli grow well in culture tubes containing slants of glycerol agar or egg medium (Petroff's) without regard to whether the tubes have been capped with waxed cloth or with tin-foil securely held in place with rubber bands, thus indicating a ready access of atmospheric air in the folds of the tin-foil in spite of precautions to prevent this means of the escape of the carbon dioxid produced by the respiration of the bacilli. Tin-foil capping, therefore, does not account for the low percentage (27.3%) of positive cultures

obtained by Corper, Fiala, and Kallen in cultivating microscopically positive sputums. The addition of "aminoids," beef or casein, to the ordinary laboratory glycerol broth has no appreciable effect on the growth of human tubercle bacilli on this medium; such an addition may even markedly retard the growth of the bacilli, as was found to be the case with beef "aminoids."

(1d—99)

(1d—99)

**Method for Making a Rapid Homogeneous Culture of the Tubercle Bacillus.**

*A. Vaudremer, Compt. rend. Soc. de biol., 85:1055, Paris, Dec. 10, 1921.*

The bacilli grow on potato bouillon without glycerin, forming a pellicle. A fragment of the pellicle, immersed in the same medium, produces an abundant, homogeneous culture in twenty-four to forty-eight hours. The result follows equally for bacilli of bovine and human origin. The bacilli thus obtained stain with phenic gentian violet and retain the Lugol stain. They resemble the bacteroids occurring in the nodules on the roots of leguminous plants and show considerable polymorphism. The bacilli thus modified may be restored to the typical appearance by growing in a glycerinated medium for ten days. In staining with an iodin preparation, the smears must be carefully washed to get rid of starch (potato). The bacilli grown in, and modified by the glycerin-free medium are agglutinable by a human tuberculosis serum.

(1d—100)

(1d—100)

**A Modification of Ziehl's Solution for the Staining of Tubercle Bacilli.**

*K. Kerssenboom, Beitr. z. Klin. d. Tuberk., 49:105, Würzberg, Oct. 15, 1921.*

The disadvantage of Spengler's picric acid stain, which lies in its difficult focussing with the immersion lens and in the low susceptibility of the normal eye for this color tone, has been compensated by staining a second time with greatly diluted methylene-blue solution after the picric acid treatment. The technic is as follows: (1) Stain one to two minutes with hot (or 24 hours with cold) carbol-fuchsin. (2) Rinse with water. (3) Bleach with 20% nitric acid. (4) Rinse with water. (5) Treat with picric acid-alcohol, one to two minutes. (6) Bleach with 70% alcohol. (7) Rinse with water. (8) Stain with very dilute methylene-blue solution, for one or two seconds. (9) Rinse with water one-quarter minute. The picric acid content would first be used in a 0.5% concentration, as by Spengler's method, then in a 2.5% solution. (Picric-nitric acid 5.0, citric acid 10.0, distilled water 85.0, absolute alcohol 100.0.) A fading of the stained tubercle bacilli was not observed. The second coloring was made with a 0.005% methylene-blue solution. The numerical similarity, according to Gaffsky, in more than 300 prepared tests showed the superiority of this staining method. The far-reaching elucidation of the slides unites, with the ease of making the immersion, the advantages of both methods.

(1d—101)

The Bactericidal Action of Gastric Juice on *Bacillus Tuberculosis*.

*John Inkster and S. Roodhouse Gloyne, Brit. M. J., London Dec. 17, 1921, p. 1024.*

Gastric juice was removed in fractions from normal individuals after an oatmeal test—meal, and tubercle bacilli, in sputum and in mouth washes, were exposed to it for from ninety to one hundred and eighty minutes. The fractions, which varied in total acidity from 24 to 62, were inoculated into guinea-pigs after neutralization, and the disease developed in 10 out of 13 animals. The protection against the tubercle bacillus by the gastric juice is apparently by no means perfect, although dilution of contents and motor activity in the stomach are probably important factors in defense.

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(1d—102)

Susceptibility of Rabbits to the Virus of Measles: Inoculations with Nasopharyngeal Material.

*M. Grund, J. Infect. Dis., 30:86, Jan., 1922.*

Grund's investigation was undertaken to determine whether or not the inoculation of nasal secretions from patients with measles would produce definite and characteristic symptoms in rabbits. The majority of rabbits gave a certain reaction, but there appeared to be a fairly large number of refractory individuals. In a number of instances, only 1 animal of 2 inoculated with the same nasal washings developed symptoms, and even when both succumbed, there was often considerable difference in the severity of the symptoms. The incubation period in susceptible animals lasted from two to seven days. While it cannot be claimed that in any one animal a typical picture of measles was obtained, yet Grund thinks that the results indicate that rabbits are susceptible to the virus of measles and, within rather wide limits, give a characteristic syndrome.

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(1d—103)

Virulence of the Cerebrospinal Fluid in Herpes Genitalis.

*Ravaud and Rabeau, Compt. rend. Soc. de biol., 85:1132, Paris, Dec. 17, 1921.*

The cerebrospinal fluid of 5 cases of herpes genitalis was inoculated into the corneas of 5 rabbits. The results obtained in one of the tests are as follows: The herpes was of neuralgic type. The cerebrospinal fluid gave a distinct cellular reaction and contained 0.50 albumin. The Wassermann and benzoin reactions were negative. In a few days, the corneal scarification entirely disappeared. Nervous signs were noticeable fifteen days after inoculation. They gradually decreased, but the animal died forty-three days after inoculation. No visceral lesion was found. The nervous system presented slight irritation of the pia, prolonged down the septa. No acute encephalitis. Some of the vessels in the gray and white matter of the cerebellum, aqueduct of Sylvius and the mesencephalon were surrounded by sheaths, identical with those of human experimental encephalitis and herpetic encephalitis. There was an abscess about the aqueduct of Sylvius. Cultures from the brain were positive. They were kept in glycerin for twenty-eight days and inoculated intracerebrally into another rabbit, now under observation.

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Liquid from the herpetic vesicles of the same case concerned in the test described above produced typical keratitis in another rabbit on the third day, followed, on the seventh day, by encephalitis. It therefore appears that the same herpetic virus is present in the vesicles and cerebrospinal fluid.

(1d—104)

(1d—104)

**The Relation of the Virus of Febrile Herpes to the Virus of Encephalitis Epidemica.**

*R. Doerr and A. Schanbel, Ztschr. f. Hyg. u. Infektionskr., 94:29, Berlin, Oct. 12, 1921.*

Doerr and Vechting corroborated the statements of Grueter and Loewenstein that in all cases of human herpes, not only of zoster, the vesicle contents produce typical vaccination herpes on the rabbit's cornea which is followed by a local immunity to subsequent inoculation with herpes of any kind. This indicates that the causative agent of all kinds of herpes is identical.

It has been observed recently that vaccination herpes is not always a purely local affection, but is sometimes accompanied by general symptoms, including typical cerebral manifestations. Doerr and Voechting succeeded in producing this general infection in a rabbit by intravenous injections of large quantities of virulent conjunctival secretions. The emulsified cerebral substance of a rabbit thus inoculated, when injected subdurally into another rabbit, produced the same disease. The authors point out the analogies between this picture and that of human encephalitis lethargica, and its resemblance to the virus of encephalitis of rabbits. In rabbits inoculated intradurally there is a shorter period of incubation than after corneal vaccination, in most cases this is only five or six days, rarely eight days. But a short incubation sometimes occurs also in corneal infection (in 4 cases six to eight days), this shows that the virus does not undergo any change when inoculated into nervous tissue, but that the prolongation of the incubation period is caused by the transmission of the virus from the eye to the brain by way of the lymph and blood. Only 13% of corneal vaccinations caused cerebral manifestations, this being due not only to the degree of virulence of the virus, but also to the susceptibility of the animal; the latter factors also decide the severity of the corneal affection. General infection is only produced in cases of a severe involvement of the cornea. Doerr and Voechting have demonstrated that, although unilateral keratitis caused by vaccine does not produce immunity of the second eye, it causes an attenuated infection, not accompanied by general symptoms. The virulence of the different species of herpes varies considerably and remains constant throughout many transplantations. Corneal inoculation with the weakly virulent species never causes general infection.

The virulence of the herpes is independent of the nature of the basic febrile disease. This proves that herpes is an independent process not affected by the basic disease. It is not known why herpes frequently accompanies certain diseases (cerebrospinal meningitis), and rarely accompanies other diseases (typhoid fever), and why it is impossible to effect herpetic inoculation upon the human or the rabbit skin. While a general infection following upon corneal inoculation is sometimes cured, infection after dural vaccination is always fatal. The protracted course of the disease after corneal vaccination (two to seven days), as

compared to dural infection (twenty-four to thirty-six hours), afforded a better study of the symptoms. It is noted that resulting paralyses frequently recede, similar to the ocular paralysis of human encephalitis lethargica. In both cases the fatal outcome is not prevented by a recession of the paralysis, as it probably depends upon a simultaneous involvement of other important parts of the brain. The transmission of the virus along the optic nerve cannot be accepted, as seven days after its introduction into the eye (anterior chamber) the vitreous and retina were not infected. Hematogenous transmission of the virus is supported by the production to general infection through intravenous injection, and successful corneal inoculation with the blood of infected rabbits. Typical corneal infection sometimes appeared spontaneously in animals inoculated intravenously.

Rabbits inoculated durally have typical fever curves; about ten hours after trephining, the temperature rises about  $1^{\circ}$  and remains constant for several days; then another sudden rise of  $1\text{--}1.5^{\circ}$  occurs. When the spasms and paralysis are at their height, the temperature rapidly drops (to  $36^{\circ}$ ). This hypothermia lasts until death. Certain analogies between these curves and those of human encephalitis lethargica are interesting. Even though the latter has no typical fever curve, a fall in temperature occurs when the paralytic phenomena are at their maximum.

It is possible that the temperature variations depend upon an elective affection of the temperature centers in the diencephalon, analogous to the affinity of the virus of lethargic encephalitis for the nucleus of the motor oculi. In both diseases the antagonism between the nerve phenomena and the fever support the assumption that the latter does not depend upon a pyrogenic toxin, but upon a local affection within the centers that regulate temperature.

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(1d—105)

**Experimental Epidemic Encephalitis Produced in the Rabbit  
by Virus of Cerebral Origin.**

*C. Kling, H. Davide and F. Liljenquist, Compt. rend. Soc. de biol., 85:1182, Paris, Dec. 17, 1921.*

The rabbit has been proved most suitable for inoculation experiments with encephalitis lethargica. However, the animal has great natural resistance and infection produces relatively mild effects. Although the resulting development may be rapid, it is usually slow. In a rabbit inoculated with cerebral substance obtained from a typical case of the disease, the course continued for nine days with practically no signs except fever. Typical cerebral appearances were found at autopsy, after the animal was killed. Had it been allowed to follow a natural course, it is very likely that the infection would have been successfully resisted. This supposition is supported by the fact that it proved impossible to transfer the disease from the first test animal to others. Besides mononuclear infiltration, an acute process, with polynuclear accumulations, has been noted. A purified virus has been obtained, cultivable in vivo. After passage through the brains of 5 rabbits, the new virus produces infection developing in the same slow manner as that just described.

(1d—105)

(1d—106)

**Experimental Epidemic Encephalitis Produced in the Rabbit by Virus of Nasopharyngeal Origin.**

*C. Kling, H. Davide and F. Liljenquist, Compt. rend. Soc. de biol., 85:1186, Paris, Dec. 17, 1921.*

Washings of the nasopharynx, in a typical case, were concentrated from a volume of 300 c.c. to 25 c.c. Similar material was obtained from 3 cases, occurring in the same family. A rabbit inoculated with the virus first described died spontaneously about seven months after being infected. Appearances characteristic of encephalitis were present, chiefly in the mesencephalon. A second animal, inoculated with virus obtained from the first rabbit, died spontaneously in four months. The histologic changes were the same. A rabbit inoculated with the virus representing the 3 cases presented cerebral symptoms and coma three and a half months after inoculation. This animal was killed while comatose. From a second rabbit, inoculated at the same time as the other with the same (second) virus, inoculations were made into a third. This third animal died spontaneously in two and a half months. The virus thus seemed to have been rendered more virulent by passage through the animal. The experiments illustrate the slow course often occurring in encephalitis lethargica.

(1d—107)

**Protozoal Absorption and Overton's Membrane.**

*B. Sokoloff, Compt. rend. Soc. de biol., 85:1102, Paris, Dec. 10, 1921.*

The relation of osmotic pressure to cell life is not universally considered important. There is also difference of opinion as to the existence of a semipermeable membrane. Studying regeneration and segmentation in protozoa, the author has become convinced that there is at least a function comparable to that of a real semipermeable membrane. His experiments were made on Stenophora juli, Nina gracilis, Gregarina cuneata and other gregarines. These parasites possess a gelatinous, subcutaneous layer, surrounding the entire structure except the first segment (protomerite). In the entire gregarine, not divided segmentally, iron is absorbed only by the protomerite, though also by the second segment after a long time. If the gregarine is cut into sections, iron is still absorbed only by the protomerite, since the protoplasm contracts about the cut area and prevents the entrance of substances from without. By altering the reaction of the medium, the usual results are entirely changed. Iron can enter the cut section, under the new conditions, more readily than it can pass into the protomerite. Absorption of iron by the gelatinous substance occurs normally if the concentration is weak. These facts can be explained only by the existence of a semipermeable membrane.

(1d—108)

**A Note on the Venereal Spirochetosis of Rabbits. A New Technic for Staining Treponema Pallidum.**

*Hideyo Noguchi, J.A.M.A., 77:2052, Dec. 24, 1921.*

Some instances of venereal spirochetosis of rabbits have been recorded in England (1913), later in Austria, Germany and Holland, but up to the present none have been recorded in America. In June, (Sec. 1—Page 325)

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1921, among 50 rabbits of the so-called normal stock of the Rockefeller Institute, the writer found 3 females and 2 males which had spontaneous lesions of the anogenital region containing an organism resembling *Treponema pallidum*. In November, among 20 rabbits purchased in Pennsylvania, 6 females had similar lesions.

In the writer's laboratory, a new procedure has been worked out by which both *Treponema cuniculi* and *Treponema pallidum* can be stained distinctly, not only with Giemsa solution but with basic dyes. One part of formaldehyd solution in 9 parts of phosphate buffer solution is used as a fixative, the scraping or tissue emulsion being suspended in small amount of buffered formaldehyd solution and the mixture allowed to stand at least five minutes (the longer the fixation, the better the results). Thin films are made on clean slides and dried in the air; the film surface is flooded with saturated alcoholic solution of gentian violet or fuchsin. The slide is immediately washed in running water and air-dried. If amount of material is small, a drop of the fixative may be put on a slide and a drop of the exudate added; the mixture allowed to stand for five minutes or longer (protected from evaporation), and then spread on a very thin film.

The fact that serums of rabbits harboring large numbers of *Treponema cuniculi* in genital lesions, even for as long as five to six months, give negative Wassermann reactions, while, with the blood of rabbits having scrotal chancres, strong positive reactions are obtained, is rather striking.

(1d—109)

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**A New Spirochete, Spirochaeta Perforans, Constantly Present in Alveolo-dental Polyarthritis.**

*Cavalié and Mandoul, Compt. rend. Soc. de biol., 85:1068, Paris, Dec. 10, 1921.*

The authors reported a series of 23 cases in which they found the new species and, since the first report, they have verified their earlier findings. The parasite is found at the junction of diseased and healthy tissues. It is 10 to 13 microns long and about 2 microns thick. The extremities do not taper, but end abruptly, without flagella. The parasite may have 3 to 5 or 7 to 9 spirals. In the former case, the amplitude is large and the height of the spiral is small; in the other condition, the height of the spirals remains the same but the latter are obviously more closely wound. Besides the location mentioned above, the authors find the spirochete in the bony alveolar tissue, in zones of rarefying osteitis, in the alveolar cavity and in exudates from the alveolar cavity. In the last two situations, it is more or less masked by other organisms. It has not been found within the roots or root-canals. It is also absent in cases of chronic, purulent or nonpurulent mono-arthritides. Since it occurs in situations most advanced toward the healthy tissues, the authors regard it as the cause of expulsive polyarthritis.

(1d—110)

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**Spirochetal Organisms in the Tissues in Acute Yellow Atrophy of the Liver.**

*N. Hayashi and T. Kibata, J. Infect. Dis., 30:64, Jan., 1922.*

Hayashi and Kibata were able to demonstrate the occurrence of a species of spirochete in the liver and certain other affected organs from (Sec. 1—Page 326)

a typical case of acute yellow atrophy of the liver. The 3 types observed are believed to represent stages in the life cycle of a single species. On the basis of these findings alone the etiologic relation of the spirochete to the disease cannot be considered as definitely established, but in view of the fact that the organism was most abundant in the liver where the lesion was most prominent, and less abundant in the intestines, kidneys, and pancreas, which showed only slight lesions, it is conceivable that there may be such an etiological relation. As a general rule, it may be stated that the relative abundance of an etiologic agent is parallel with the degree of severity of the lesion.

(1d—111)

**Four Parasites of the Field Rat or Muskrat (*Microtus Arvalis* Pallas).**

(1d—111)

*G. Lavier, Bull. Soc. path. exot., 14:569, Paris, Nov. 9, 1921.*

The field or muskrats examined are burrowing animals destructive to crops and native in the vicinity of Dijon. The parasites found were as follows: (1) A hemogregarine, identical with that observed by Martoglio and Coles, and for which the name *Hemogregarina arvalis* has been suggested. The parasite is cylindrical and 5 to 10 microns long by 4 microns in diameter. The nucleus is granular and compact; the average dimensions are 5.2 microns by 2.8 microns. The parasite occurred in the large mononuclear leukocytes and in smears made from the lung. It was infrequent in liver smears and absent in smears from the spleen, bone marrow and kidney. Schizogony was noted in lung sections stained by Giemsa's stain or hematoxylin. Other preparations were fixed by the May-Grunwald method and stained by Giemsa. The author hopes to describe the ectoparasite which acts as intermediate host. (2) A *Grahamella* was found in a few red cells and free, after liberation from the erythrocytes. Such occurrence free is rare and may possibly be due to rupture produced by making the smear; but it also suggests schizogony. The single animal in which the parasites were found appeared healthy; the usual anisocytosis and polychromatophilia were present and the blood contained a few normoblasts and abundant Jolly's organisms. The *Grahamella*, when found free in the blood, resembles *Rickettsia*. The author suggests the name *Grahamella microti*. (3) A spirochete was abundantly present in lung smears and more rarely in smears made from the liver. The parasite is short, thick and has only 2 or 3 spirals. The dimensions are 3 to 4 by 0.25 microns. The spirochete corresponds to the description given for *Treponema minus*. The latter is probably identical with *T. morsusmuris*. The French animal may therefore possibly be a means of conveying rat-bite fever (sodoku). (4) Besides *Hemogregarina arvalis* and *Grahamella microti*, one of the animals also contained a trypanosome. The latter corresponds to *Trypanosoma microti*, as described by Laveran and Pettitt, except that the dimensions are slightly greater. Measurements are given in detail. Inoculation into other animals failed because of immunity. A bibliography and drawings accompany the article.

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(1d—112)

New Coccidia Parasitic on Carp.

S. Stankovitch, *Compt. rend. Soc. de biol.*, 85:1128, Paris, Dec. 17, 1921.

Three new forms of the coccidia, studied at the fisheries' laboratory of the University of Grenoble, are described: (1) *Eimeria cyprinorum*, n. sp. This organism is widely distributed in France, occurring in the intestinal epithelium of a number of species of the carp family. The hosts are the young fish. They do not seem to suffer particularly from the presence of the parasite, but do not appear so vigorous as normal. The schizonts are ovoid, 11 to 12 microns long, and produce merozoites. The oöcysts are numerous. The mature oöcyst is spherical, its walls are thin and hyaline and the cyst does not remain; its diameter is 12 or 13 microns. The spores are 4 in number and 7 to 8 by 5 microns. (2) *Eimeria cylindrospora*, n. sp. In spring and summer the species may be found in the intestinal epithelium; it infests the young fry of *Alburnus lucidus*, of the lake of Aiguebelette, in Savoy. By autumn, the host appears to get rid of the parasite. Sporulation has been observed, but not schizogony. The ripe oöcyst is spherical, with thin hyaline walls. The diameter is 10 to 11 microns. The spores are thin walled, and contain each 2 sporozoites. They measure 7 to 8 by 4 microns. The spores are always grouped in pairs, usually parallel. (3) *Eimeria soufiae*, n. sp. This species produces a fatal enteritis in the young of *Squalius agassizi*. It is relatively large. The ripe oöcyst is 17 to 18 microns in diameter, and contains 4 spores. The walls of the oöcyst and spores are thin. The spores measure 11 or 12 by 6 microns. The species somewhat resembles *E. subepithelialis*, but its spores are smaller and have thinner walls.

(1d—113)

A New Gregarine Parasite (*Lankesteria cyclopori*, n. sp.) of *Cycloporus maculatus* P. Hallez.

R. Poisson, *Compt. rend. Soc. de biol.*, 85:967, Paris, Nov. 26, 1921.

Many individuals of *Cycloporus maculatus* Hallez collected during the summer of 1921 at Luc-sur-Mer (Calvados) had numerous Gregarine, monocystic parasites. The length of the sporozoite is 4.5 to 5 microns. It penetrates a cell of the host's intestinal epithelium, enlarging to a length of 20 to 30 microns, further development often occurring within the intestinal lumen, the parasite remaining free or becoming again attached to an epithelial cell. The adult measures 90 to 120 by 20 to 25 microns. The nucleus is nearly always anterior. Protection is afforded by a thick cuticle, readily detachable from the cytoplasm by drying. Cysts are formed after conjunction, which occurs within the lumen of the intestine. Other characters, illustrated by drawings, are described in detail and allow this species to be included provisionally among *Lankesteria*. The parasite is named *cyclopori*, n. sp. The genus in question requires further study and revision.

(1d—114)

The Host of *Leposphilus Labrei* Hesse.

L. Mercier, *Compt. rend. Soc. de biol.*, 85:897, Paris, Nov. 17, 1921. On account of confusion in the terminology, the question of the (Sec. 1—Page 328)

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host should be reviewed to determine, whether, in fact, there are 2 hosts or but 1. *Labrus* has been mentioned as the host. The author has found *Leposphilus* on *Crenilabrus melops* L. In *Labrus*, the borders of the preoperculum are smooth, while they are dentate in *Crenilabrus*. This fact should prevent confusion. Parasitic tumors described by Hesse as occurring usually on the right side, occur indifferently on right and left. Instead of lying above the lateral line, the author finds them exactly on the lateral line. Within the tumors, there are 2 or 3 deformed and excavated scales sheltering the parasites, one scale invariably lying in the lateral line. Parasites appear to prefer the scale so situated. Three parasites have been found in the same cavity. *Leposphilus* appears to vary in frequency from year to year. None were found at Luc in 1920, while they were relatively abundant in 1921.

(1d—115)

(1d—115)

### The Intermediate Host of *Schistosomum Hematobium* in Portugal.

*A. Bettencourt, I. Borges and A. de Seabra, Compt. rend. Soc. de biol., 85:1169, Paris, Dec. 17, 1921.*

Cercaria of *Schistosomum hematobium* have been found in *Planorbis* at Atalaia, Portugal, as previously reported. The morphology has been studied further and the authors' findings confirm those of Cort and Faust. It seems clear that the intermediate host, in Portugal, is *Planorbis corneus*, var. *metidjensis* Forbes. Attempts to secure infestation of other mollusks failed. Bilharziosis in Portugal seems to be wholly referable to the village of Santa Luzia, near Tavira, or to Tavira. The infestation occurs in women of these places; it is especially noticeable in laundresses who remain in the pool of Atalaia for considerable periods of time and thus receive the parasite from *Planorbis*. The pool is but 40 to 50 cm. deep. Adaptation of the cercaria to other than the usual host appears to be indicated by the facts reported.

## 1e. IMMUNOLOGY, SEROLOGY AND HEMATOLOGY

(1e—135)

(1e—135)

### Nonspecific Immunity.

*Hans Much, Hygiea, 83:785, Stockholm, Dec. 16, 1921.*

The author believes that it is an error to consider the manifestation of a disease alone as the most important factor in preventive therapy. Bactericidal serotherapy and chemical sterilisatio magna are mistakes. It is much more important to give attention to the defensive powers of the body, and their reinforcement is the most important task of medicine. Immunity is not restricted alone to the form of specific immunity phenomena. Every strengthening or weakening of the cells is an immunogenic process. The blood phenomena are most frequently indicators of the cellular function. The author considers various diseases to be disturbances of balance between attacking powers (irritation) and the defensive powers (the body). It is therefore necessary to strengthen the defensive powers of the body. This strengthening is accomplished by means of immunization. The immunizers are either specific or nonspecific. The immunizers affect both the serum of the blood and the cells. There exists, therefore, both a humoral and a cellular biology.

All therapy has therefore a biologic basis, or is, in respect to its purpose, biologic or immunotherapeutic. Biologic therapy may be grouped in 3 groups: (1) biologic isotherapy, in which the virus itself is employed for stimulating immunity; (2) biologic homeopathy in which the virus and related elements are employed for stimulating immunity; and (3) biologic allopathy in which matters foreign to the virus of the disease are employed for stimulating immunity. By means of all of these 3 immunizing methods, both specific and nonspecific immunity may be produced, and the author considers them all to be purposive. The selection of the most suitable of these methods depends upon the specific cases of disease.

The prophylaxis and the therapy need not necessarily be based upon the same theory. In the same disease the prophylaxis may most effectively be based upon specific and the therapy upon nonspecific immunity, or vice versa. It is necessary that the specific and the nonspecific immunity should not be confused. The nonspecific therapy may affect the specific as well as the nonspecific immunity, and the nonspecific immunity may be changed or strengthened not only by means of nonspecific means but also by specific means.

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**A New Conception of Phenomena of Immunity.**

*P. Rondini, Riforma med., 37:1124, Naples, Nov. 26, 1921.*

The author criticizes the ideas put forward by Herzfeld and Klinger (which are not new, but are an exposition, in a new form, of an older concept) that antibodies are the result of a transformation of antigens. This has been successfully combated by the classic opinion that antibodies represent a reaction of the organism, a species of secretion of the body-cells, under the stimulus of the antigens. The fundamental objection to these authors' conception is that already made to Buchner, whom they follow; how can a small quantity of antigens produce a quantity of antibodies many times superior to that required to neutralize the antigen injected? Their assertion that the antigen exfoliates so abundantly as to transform into antibodies a large part of the proteins of the plasma is purely hypothetical, as is also their sophistry that these antibodies become stored in determined tissues, from which they can be turned back into the circulation, a theory which they were forced to invent to explain the well-known fact that the production of antibodies can be increased, or reactivated, by aspecific stimuli. This fact finds its natural explanation in the classic doctrine that sees in the antibodies products of fabrication (especially of secretion); but it is not accounted for without a straining of logic, by positing an origin of antibodies from antigens. The ideas of Herzfeld and Klinger may be useful as a basis of further research, but their hypothesis calls for too many supplementary admissions, and does not correspond to Mach's law of "economy of thought."

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**The Action of Bacterial Culture Products on Phagocytosis.**

*Augustus B. Wadsworth and E. N. Hoppe, J. Immunol., 6:399, Nov., 1921.*

Experiments were undertaken for the purpose of investigating further the action of the known bacterial poisons on the body cells, and  
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in the hope of finding some isolated animal cells or tissues sensitive to the unidentified bacterial substances, and a technic delicate enough to register degrees of injury to their normal reactions. Leukocytes were used in the tests. After many preliminary studies a very simple technic was evolved. In general the method consisted of exposing well washed leukocytes to the action of the substances to be tested. The effect of this exposure was then measured by the degree of phagocytosis that occurred when sensitized staphylococci were brought in contact with the leukocytes. This degree was determined from microscopic preparations, and stated in units as the phagocytic index. Each operation was standardized. The action of culture broths of 13 widely differing pathogenic and saprophytic bacterial species was tested on phagocytes in vitro. A table shows that in every case the phagocytic power of the leukocytes was inhibited in a high degree. In the second series of experiments facts regarding the nature of this depressing substance in toxins and culture broths were determined. Diphtheria toxin was generally used and the previous technic was again employed. The tests fell into 4 groups: (1) the effect of the time of exposure, (2) the effect of neutralizing agents, (3) the effect of destructive agents, (4) the source of the depressing factor. These tests showed that its action was immediate, and could not be neutralized by the ordinary antiserums tested, nor destroyed by exposure to the degrees of heat or light used. The composition of the medium, which is most important in true toxin production, in no way affected the production which depressed the phagocytic index. All of the toxins used were equally depressing. Older cultures produce the depressing substance more markedly than do younger cultures. This is an important factor in the production of the depressing substance. This substance is either wholly or partially destroyed by digestion of proteolytic enzymes. This substance has already been isolated from standard diphtheria toxin by adsorbing it to leukocytes and then lightly washing it from them with physiologic salt solution. The phagocytic activity of the leukocytes can be regained by removal of the substance.

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**The Precipitation and Concentration of Substances Having the Function of Antibodies.**

*G. Izar and G. Caruso, Riforma med., 37:1123, Naples, Nov. 26, 1921.*

All biological reaction between the so-called antigens and immune serums are disturbed in the latter by the presence of substances with aspecific function which may hinder or simulate the awaited reaction. Many attempts have been made in vain to get rid of these. The author has undertaken to establish their behavior in contact with various quantities of water double-distilled in the presence of soda. He confined his experiments to bacterial agglutinations, hemolysins, and the antibodies contained in syphilitic serums having a positive Wassermann in the presence of leutic antigens. He showed that it is easy in this way to separate from the blood-serum substances endowed with specific properties in the presence of their respective antigens. Up to a certain point, the quantity of antibodies precipitated parallels the quantity of distilled water added; beyond this point, the addition of water begins to cause the precipitation also of substances with aspecific power. Results vary

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with different kinds of antibodies. Thus, for hemolytic antibodies, the best relations were found when the volume of serum is 3 to 4 times that of distilled water; for agglutinating antibodies it is more than 1:30; for those capable of fixation of complement, in the presence of a leutic antigen, it is about 1:5 or 1:7, varying with the serums, because, in this case, when we increase the volume of water, we also increase the substances endowed with aspecific power to inhibit. The author did not succeed in establishing results on precipitating antibodies, because the serums, by action of the distilled water, assume an opalescent tint that hinders the reading of the results.

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**Formation of Antibodies in Thyroidectomized Animals.**

*B. Housay and A. Sordelli, Compt. rend. Soc. de biol., 85:1220, Paris, Dec. 17, 1921.*

A previous report was obscured by the omission of certain statements. The complete conclusions are as follows:—Hemolysins: anti-sheep serum obtained from thyroidectomized rabbits contained more of these substances than that of the control animals. Immunization was intravenous. Agglutinins: More in thyroidectomized rabbits and horses than in the controls. Antitoxins: Thyroidectomized dogs furnished the more active antidiphtheritic and antitetanic serums. Sometimes there was not much difference. Thyroidectomized horses and rabbits furnished much more active antidiphtheritic and antitetanic serums than those obtained from the controls. Toxins were always injected subcutaneously. Whether these differences depend on species, diet or manner of immunizing, remains to be determined.

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**The Specific Antigenic Properties of the Four Groups of Human Erythrocytes.**

*Sanford B. Hooker and Lillian M. Anderson, J. Immunol., 6:419, Nov., 1921.*

(1) Mechanism of human isoagglutination: appropriate absorption tests show that Landsteiner's theory is probably correct. The question of the existence of subgroups is still open. Data is submitted in support of the recommendation that both the typing of bloods and direct tests between recipient and prospective donors be adopted as routine procedures preliminary to transfusion. A number of observations are presented which arouse suspicion, at least that blood plasma rather than cells may be the source of certain posttransfusion reactions. The writers were unable to demonstrate any isoprecipitins or alexin-binding antibodies in cross-titration of representative group serums, therefore they conclude that there is probably no etiologic or concurrent antigen-antibody plasma reaction following primary transfusion. They believe that both from the clinical standpoint and because of the information which would derive to the subject of antigenic specificity, that serologic methods deserve more thorough application, particularly to the problem of those reactions which follow repeated transfusions.

(2) In order to simplify interpretation of results by reducing the number of variables as found by other workers, the writers used cells of only one normal individual of each group for the production of immune serums. The method of injecting rabbits and dosage of injection is

given. It was found that normal rabbit serums possess weak agglutinins for the 4 groups of human erythrocytes. In certain rabbits, this agglutinative capacity is group-specific, being particularly marked for groups II and IV cells. These 4 types of human serums also contain agglutinins for rabbit erythrocytes, but there is no group-specificity evidenced. The rabbit cells adsorb human isoagglutinin "b," present in group I and II serums. By using appropriate adsorption, the group-specific hemagglutinins were produced by the injection of rabbits with type cells. Cells of group I, from certain individuals, were found to contain a specific agglutinogenic component that does not exist in the other group cells examined. Group-specific hemolysins or alexin-binding antibodies are developed with the agglutinins. The writers stress the fundamental importance of the animal's individuality in its bearing on serological studies. In the experiments, a number of animals did not produce group-specific antibodies and the cause for this variation was not determined. Tables are given which show the various serological tests.

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**On the Structure of Opsonic Complement.**

*M. Kodama, Japan Med. World, 1:9, Tokio, Nov. 15, 1921.*

It is an established fact that tropin and opsonin in an immune serum are the substances which prepare bacteria for phagocytosis of the white corpuscles. The actions of cells on bacteria and the part which opsonin takes in their struggle, and in the phenomena of phagocytosis, have been extensively investigated. Certain criticisms of the methods employed by various investigators are here offered as explaining to a degree the variations in results. In the present experiments, the method of Wright was modified to eliminate the objectional features and to supply other factors: After determining the absence of tropin in an immune serum, it was diluted 100 times; then were added an equal amount of complement diluted 60 to 80 times, then the white corpuscles and bacteria emulsion, and the mixture was incubated for 15 minutes at 37°. The material so prepared was placed in a clean Petri dish, and with a rubber-capped Wright capillary pipet, the same amount of corpuscles, amoebaeceptor, complement and bacteria emulsion were sucked up. Equal quantities of each, secured in this way, were mixed thoroughly by repeatedly drawing them in and out of the pipet upon a paraffined Petri dish. The mixture was then drawn into the pipet and the end sealed with flame. This was placed in a water bath at 37° for fifteen minutes. After the incubation the content was placed on the paraffined dish; a smear slide was made with a portion of the mixture and fixed by placing it in methyl alcohol for ten minutes, then stained with Otani's azuroeosin. Liefmann's carbon-dioxid precipitation method was used to separate opsonin complement from the fresh serum of a rat. Results show that opsonic complement can be separated into a midpiece and an endpiece; that the endpiece contains more of the complemental element than the midpiece; that the complemental action of both pieces is destroyed by heating at 55° for thirty minutes. The complement also contains the third component, as shown by the following observations: When the serum is agitated (18 times per minute) for sixty minutes the complemental action is lost. The complemental action is revived when agitated serum is added to inactivated serum, by heat. The quantity of complemental element contained in the third component is midway

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between the midpiece and the endpiece. The action of opsonic complement is produced by the concerted action of the three constituents; each constituent alone has very weak or no complemental action. The structure of opsonic complement, therefore, resembles that of hemolytic complement, though both cannot be said to be the same.

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**An Introduction to the Study of Hematophagy.**

*H. M. Woodcock, J. Roy. Army M. Corps, 37:418, London, Dec., 1921.*

In his former article Woodcock showed that the lymphocytes of the guinea-pig customarily devour red corpuscles, but, unlike the macrophages, are unable to assimilate this food and only alter it into a Kurloff-body. Nevertheless, the fact that these cells may be hematophagic immediately suggested to his mind the possibility of certain other types of cells—other than blood cells—behaving similarly, under abnormal conditions. The Kurloff bodies have often been compared, in a general way, with Negri bodies and similar formations. Negri bodies were therefore studied. A regular series of transitions can be found between what are undoubtedly red corpuscles or corpuscular masses, and fully formed Negri bodies. The whole transformation into a Negri body, may, on occasion, take place really extracellularly, while the blood is still in a narrow capillary segment. From the evidence presented it is apparent that the various appearances presented by the Negri body can be readily correlated with those of the Kurloff bodies when they are similarly stained (iron-hematoxylin and eosin). It must be remembered, however, that the hematophages concerned in the two cases are of quite different order: in the one case, a nerve cell and in the other, a lymphocyte. The chief differences between the Kurloff bodies and the Negri bodies is due to the iron compound, separated from the protein elements, being in a somewhat different condition in the two cases. In the Kurloff bodies, it is in a more liquid condition, and constitutes a practically spherical globule. In the Negri bodies, the corresponding substance is more solid and may retain the shape of the original corpuscle. The varying size of the Negri bodies depends entirely on the amount of corpuscular material ingested by the nerve cell, in the same way as does the size of the Kurloff body. Guarnieri's bodies, occurring in the epithelial cells in small-pox and vaccinia, are generally agreed to be bodies of similar character and to originate in the same way as Negri bodies. They equally have been included in the Chlamydozoa, under another imposing name. There is no doubt whatever that these, too, are simply the result of epithelial cells becoming hematophagic, with consequences of the same order, namely, alteration, but not digestion and assimilation of ingested material. The same explanation may also apply to the case of the bodies in "Molluscum contagiosum," trachoma, Mallory's bodies in scarlet fever, etc. In short, the writer wishes to express his considered opinion that Prowazek's entire conception of the Chlamydozoa, with their "elementary corpuscles" "initial bodies" and all the complicated phases of their life cycle, will be proved to lack reality and must be banished as an illusion. At any rate there are no such parasites or parasitic complexes as "Lymphocytotozoon cobayae," Leuko-cytozoon (sic!) syphilidis" and many of the intracellular phases intercalated by certain authors into the life cycle of *Treponema pallidum*.

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"Neurocytes hydrophobiae" and "Cytrocytes variola" and "vaccinae." Lastly Woodcock suggests that the parasites that have been described under the name of Rickettsia, occurring in typhus, and the very similar ones occurring in Rocky Mountain spotted-fever, a closely allied disease, are also to be regarded as granular formations produced as a result of hematophagy; in other words, that the minute bodies hitherto found in cases of these diseases and placed in the above category have, in reality, nothing of a parasitic or organismal nature about them. But it is quite possible that these formations bear some fundamental etiological relation to the disease. They may hold the secret of the pathology though they are not parasites. The etiological agent which starts hematophagy is some ferment which stimulates fresh cells of the same type to hematophagy and the production of more of this same substance. The metabolic processes in connection with hematophagy will supply the "multiplicative" factor. Thus inoculation will lead, after an incubation period, to the development of the visible signs and symptoms of disease. More and more of the virus will be developed until, in a favorable case, antibodies developed in response are sufficient to counteract it.

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**Effect of Temperature on the Bacteriophagus.**

*F. d'Herelle and E. Pozerski, Compt. rend. Soc. de biol., 85:1011, Paris, Dec. 3, 1921.*

Various students have attempted to determine the critical point of inducing lysis of a bacterial emulsion by the heated culture. Simple lysis is not positive and may lead to false conclusions, since it may be produced only by very active strains of the bacteriophagus; weaker strains, though not producing lysis, may still be present. In the absence of lysis, presence of the weaker strain may be shown by placing upon inclined gelose a drop of the emulsion not showing lysis; the bacteriophage, if present, will produce circular plaques which are apparently sterile. The virulence of the strain may be raised by successive culture. For determination of the critical temperature, cultures of the bacteriophage were filtered by bougie and aspirated into fine tubes with thin walls; both ends were sealed. Eight tubes were kept at each temperature ( $60^{\circ}$ ,  $62^{\circ}$ ,  $64^{\circ}$ ,  $66^{\circ}$ ,  $68^{\circ}$ ,  $70^{\circ}$  and  $75^{\circ}$ ) for thirty minutes. The effects of the contents upon cultures of Shiga's bacillus, bacilli of Flexner and Hiss, *B. coli* and paratyphosus A and B, showed that heating above  $60^{\circ}$  produce more or less rapid attenuation. The bacteriophage was killed or rendered totally inactive by a temperature of about  $75^{\circ}$ . Twort considered that gelose cultures of the bacteriophage produce a substance destroyed by temperatures below  $60^{\circ}$ . The phenomena observed by him are not identical with those manifested under the conditions of these tests.

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**The Unity of the Bacteriophage Principle.**

*R. Bruynoghe and J. Maisin, Compt. rend. Soc. de biol., 85:1122, Paris, Dec. 10, 1921.*

Continuing their studies of the bacteriophage principle obtained from cultures of *Staphylococcus*, the authors failed to produce any effect on d'Herelle's bacteriophage in connection with Shiga, Hiss or other bacilli: 4 attempts to cultivate the principle in cultures of these

organisms were negative. They therefore believe that this principle is not identical with d'Herelle's bacteriophagus, but that possibly the question was merely one of insufficient virulence. Thorough tests were then made. They find that their principle is identical with that of d'Herelle, on the following grounds: The resistance to heating is the same (exposure for an hour to a temperature of 70° C.). Tests by alexin-fixation show that the lytic principle is the same, without regard to the bacteria affected. The principles of the authors and of d'Herelle were further compared by studies in rabbits. Deviation tests, checked by studying deviation in the presence of typhoid bacilli, dysenteric bacilli, etc., agreed for both principles. Neutralization of the bacteriolytates was carefully examined. Somewhat larger quantities of serum were required than those described by Gratia and Jaumain, but there was no doubt as to the result. Where neutralization was apparently incomplete through use of insufficient quantities, lysis occurred after seventy-two hours or more. Heating such a mixture for an hour at 56° C. failed to destroy the lytic property. The authors consider these tests conclusive evidence of the identity of the two bacteriophagous principles.

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**Determination of the Bacteriophagus.**

*R. Appelmans, Compt. rend. Soc. de biol., 85:1098, Paris, Dec. 10, 1921.*

The author suggests a method more convenient and precise than that indicated by d'Herelle. He utilizes the dilution process recommended by Miquel in water analysis. To a series of tubes containing the bacteria prepared for the action of the bacteriophagus, progressively decreasing dilutions of the latter are added. These dilutions extend in the proportion of 1 to 10, 1 to 100, 1 to 1,000, etc., up to 1 to 1,000,000,-000,000. The presence or absence of lysis indicates the presence or absence of the bacteriophagus. This result tends to confirm the theory that the bacteriophagus is a separate, living entity. The bacteriophagus, introduced into the bacterial culture, increases during incubation, whether large or small quantities be used, either of the bacteria or the bacteriophagus, and indifferently whether lysis be immediate or retarded. Centrifugation of the bacteriophagus at 8,000 revolutions per minute for an hour throws down no more bacteriophagi than the number contained in the upper layers of the liquid. If the bacteriophagus is exposed to the action of 50% alcohol or 5% carbolic acid, many of the organisms remain active, but their number is reduced. This reduction does not occur progressively and ceases at a certain point, suggesting that certain individuals are able to resist the reagents.

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**The d'Herelle Phenomenon.**

*Gildemeister, Berl. klin. Wchnschr., 58:1355, Nov. 14, 1921.*

The author reviews the results reported in the literature in regard to the "bacteriophageal" effects of stool extracts discovered by d'Herelle.

The author was led to study the phenomenon because the abnormal colony forms as described by Bordet and Cinca and obtained in cultures from the bacteriolytates of stool extracts seemed to correspond with those described by the author in 1917 under the name of "flatter" forms. If, in the stool extracts, the bacteriolytic agent employed does not suc-

ceed in complete killing of the germs, one obtains agar growths that are different from the typical colonies of the respective bacteria (typhoid, dysentery, colon bacilli) and are especially distinguished by mucous formation. The author has shown in his studies of the variability of these dysentery and colon bacilli, and to a lesser extent in typhoid-paratyphoid and paratyphoid-similar bacteria (in one case from the urine in a colon cystitis) abnormal colonies which he divides into 3 groups. The main types are distinguished by the fact that the colonies do not form regular round disks, but through defects assume irregular shapes; from normal colonies they are differentiated through their tough mucoid consistency. The second group consists of very small and delicate, flat colonies of irregular form and a dull metallic luster; they are lifted up from the medium with a loop or needle only with great difficulty. The intermediate groups represent transitions between these 2 types, ring-formed and wedge-formed being frequent. With further growth of the first type, all manner of normal and abnormal forms develop in varying numbers. The other 2 groups are equally labile; only the normal forms are stable. On account of this lability, the author named these the "flatter" forms; but even the normal forms, which are split off in the course of the growth of the "flatter" forms, can revert, after several weeks incubation, to the abnormal types.

That his "flatter" forms are identical with the atypical growths from d'Herelle's bacteriolytate, the author was able to prove by the fact that he found in his abnormal color forms a lysogenous agent of medium strength, that against both homologous and other color strains, and also against various dysentery, typhoid and paratyphoid strains was effective; and this lytic agent remained of the same strength after further cultivation. The d'Herelle phenomenon is regarded by the author as one of irritability. In experiments not yet terminated, the author was not able to show a complete solution of colon bacilli in a drop of the lytic stool extracts but he believes the bacteria after twenty-four hours were swollen and transparent.

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**Shiga Bacteriophagus.**

*Oskar Bail, Wien. klin. Wchnschr., 34:555, Nov. 17, 1921.*

The effect of bacteriophagi on Shiga's bacillus was first discovered by d'Herelle in stool extraction. As Salimbeni undoubtedly showed bacteriolytic properties toward certain myxomycetes, the claim of d'Herelle that living filterable germs are the carriers of the bacteriophagi is *a priori* not impossible. The presence of a corpuscular agent is shown by an experiment, which simultaneously allows the quantitative determination of the bacteriophagi. A plate inoculated with colon bacilli (or with other bacilli) and overlayed by colon bacteriophages, especially homologous bacteriophages, in higher concentration, shows a spot free of growth; but if the concentration of the bacteriophagi is more and more reduced, finally a dilution is reached, with which the bacterial growth on the plate no longer shows holes and whose number decreases with stronger dilutions. The strongest still effective dilution shows a hole in the plate. If a bouillon sediment of Shiga bacteriophagi, whose number was determined in the described manner, is left to stand at 37° C., their number never increases, but rather is reduced, but never to complete disappearance. But if living Shiga bacilli are added to the bacterio-

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phagi-bouillon mixture, the bacteriophagi increase, the increase being more marked and more rapid, the greater the number of the added germs; the implanted germs are destroyed the more rapidly, the greater the implantation. The number of the newly formed bacteriophagi is greater than that of the destroyed bacteria. The "virulence" of the bacteriophagi is specific.

The bacteriophagi develop (according to Bordet) in the peritoneal exudate of animals, which were injected intraperitoneally with those particular bacteria; this is not possible with Shiga bacilli. In every bacteriophage there finally develop, if the process does not continue up to the complete destruction of the germs, strains which are resistant toward the bacteriophagi. Cultures of such strains in bouillon behave as bacteriophagi in the presence of the normal strains. Finally, bacteriophagi sometimes arise spontaneously in normal bouillon cultures, if the bacteria are centrifuged off several times after a prolonged culture, the bouillon is heated to 58°, and after cooling is again inoculated with the same germs. Failure of growth in the culture shows the development of the bacteriophagi, which belong to the "small holed" form. This development of bacteriophagi in the bodies of animals and in artificial cultures shows that they arise from the bacillus itself. An antibacteriophage serum can be prepared from the bacteriophagi.

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**A Bacteriophagic Principle Obtained from *Staphylococcus*.**

*R. Bruynoghe and J. Maisin, Compt. rend. Soc. de biol., 85:1118, Paris, Dec. 10, 1921.*

The authors obtained bacteriophagic effects from fresh vaccine. The latter, planted on gelose slants, yielded colonies of *Staphylococcus aureus*, *citreus* and *albus*. Cultures were made from areas of inhibition appearing among the colonies of *S. aureus*. These cultures retarded the growth of normal staphylococci for six to eight hours. When sterilized by heating for an hour at 56° C., cultures of the bacteriophagic principle still preserved this property. Recultivation produced a bacteriophage capable of arresting the development of staphylococci for fifteen to twenty-four hours. If only a fraction of a drop of the bacteriophagic culture were added to cultures of staphylococci, normal growth of the latter was not arrested immediately. An organism was finally produced which resisted the lytic effect. The bacteriophage affected 20 different strains of *Staphylococcus*, but produced no effect on typhoid or dysenteric bacilli. The authors emphasize the contention that the staphylococcal colony from which the bacteriophagic principle was obtained consisted really of 2 varieties or strains of *Staphylococcus*. One variety was normal and ordinary, the other had a lysogenic property, or bore a parasite, according to the conception of the bacteriophage as a living organism. Testing normal cultures by heating and filtration failed to reveal any active lytic substance.

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**Therapeutic Tests with the Bacteriophagus Obtained from the *Staphylococcus*.**

*R. Bruynoghe and J. Maisin, Compt. rend. Soc. de biol., 85:1120, Paris, Dec. 10, 1921.*

Normal rabbit serum did not prevent the bacteriophage from destroying staphylococci. The same proved true for normal human (Sec. 1—Page 338)

serum. The authors made therapeutic application of this principle in 6 cases of anthrax or furuncle. Doses of 0.5 to 2.0 c.c. of bacteriolysates, sterilized by heating for an hour at 56°, were injected near the affected region. The local infiltration decreased and the lesions themselves often disappeared in twenty-four to forty-eight hours. Suppurative conditions rapidly dried up. The injections sometimes produced a slight rise in temperature. The injection-site remained painful and slightly edematous for twenty-four. The results thus far are too few to permit definite conclusions.

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**A Study of Hemoglobinophilic Bacteria by Agglutination and Agglutinin Absorption.**

*H. B. Mastland and Gordon C. Cameron, Brit. J. Exper. Path., 2:283, London, Dec., 1921.*

Study was made of 38 strains of *B. influenzae*, isolated from hospital patients during a period when no cases of epidemic influenza were seen, all requiring blood-pigment for growth. Morphologic differences did not correspond to variation in agglutination. A table gives the origin of the organisms used and the limit titer of serums. Each strain was isolated by subculturing one colony. Suspensions for agglutinating were made by washing the surface growth from chocolate agar with physiologic saline, shaking to break up the clumps, centrifuging out the coarser particles and diluting to a standard density. One-tenth per cent. formalin was added and the suspensions stored in the ice-chest. The agglutinating serums were obtained from rabbits, and had a titer of 1:1,280 or 1:2,560. For absorption of agglutinins, killed organisms were left over night at 37° C. in contact with the serum diluted 1 in 10. The strains fell into several groups. The results showed that nearly all strains of *B. influenzae* possess a serologic individuality as determined by agglutination and agglutinin absorption. Very infrequently were identical strains found. The antigenic value of strains varies. The serum prepared from such strains seldom agglutinate other organisms than the homologous. Two or more serologic races were found in the same patient.

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**Anaphylaxis in Hyperimmunizing Cattle against the Cattle Plague.**

*R. Van Saceghem, Compt. rend. Soc. de biol., 85:1105, Paris, Dec. 10, 1921.*

Hyperimmunization may readily be obtained by direct venous transfusion from an infected, to an already vaccinated, cured or immunized animal, but it is important that the procedure should not be attempted unless the animal has been vaccinated at least six months previously. If this method is used in animals which have been vaccinated for a shorter length of time, grave anaphylactic disturbances will be produced. However, transfer of blood from the vein of an infected animal to the subcutaneous tissues of an animal for which hyperimmunization is desired is without any such danger from anaphylaxis, even if the time since vaccination is much shorter than six months. Specific antibodies are still circulating in the blood of animals recently vaccinated. To employ direct venous transfusion in such animals is to surcharge the blood with

an excess of such substances. Absorption is more gradual when the blood from an infected animal is introduced, not into the receptor's vein, but under the skin. The specific substances reach the receptor's circulation in a harmless form. Symptoms of anaphylaxis may be quickly controlled, and the life of the animal saved, by intravenous injection of 5-10 c.c. sulphuric ether. The author's conclusions are based on more than 300 cases.

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**Dysentery Immunization in Rabbits by the Oral and Subcutaneous Methods.**

*S. Kanai, Brit. J. Exper. Path., 2:256, London, Dec., 1921.*

The evidence in support of oral immunization, and particularly the work of Besredka, is referred to. In view of Besredka's findings that a solid immunity may result from the oral administration of the vaccine, the writer carried out experiments on rabbits with the object of determining the degree of such resistance to *Bacillus dysenteriae* (Shiga), and to compare it with the immunity resulting from the usual inoculation.

The strains of *B. dysenteriae* used were No. 151 (Shiga) and one obtained from Besredka. Both strains were typical, culturally and serologically. The ingestion vaccines were made from a twenty-four-hour growth on agar obtained from one Roux bottle. This was suspended in 20 c.c. of sterile normal saline and heated for one hour at 60° C. Measured quantities of this suspension were mixed with bran and fed to rabbits which had fasted twenty-four hours. Tests were made for antibody production. The degree of immunity produced was determined by the intravenous inoculation of lethal doses of living *B. dysenteriae* (Shiga), the virulence of which, for the rabbit, had been previously determined. The dosage given to each rabbit is stated, together with detailed tables of the results. These show that only a small degree of immunity in rabbits by the oral administration of the dysentery bacillus resulted. Experiments to test the ingestion of living *B. dysenteriae* (Shiga) on rabbits were negative. The ingestion of bile did not seem to increase the efficacy of oral immunization. Experiments were made for comparison between the immunity produced by ingestion and by subcutaneous inoculation. Brief reference is made to the results of other work along this line. The usual method of preparing the carbolized vaccine was followed. The vaccine was delivered into the stomach by means of a small rubber cannula to which was affixed a small filter funnel. The procedure of the experiments are described in detail and the results are shown in tables. The immunity obtained by the subcutaneous inoculation of a carbolized vaccine administered in three doses of 50,100, and 100 millions is superior to that received by oral administration. Solid immunity did not result in either case.

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**Human Vaccination against Bacillary Dysentery.**

*H. Vincent, Compt. rend. Soc. de biol., 85:965, Paris, Nov. 26, 1921.*

Tests were made in 2175 subjects. The injections, though containing only 500 to 750 millions of bacilli, rapidly checked an epidemic due to Shiga's bacillus. Vaccinal immunization and production of protective (Sec. 1—Page 340)

antibodies occur not sooner than the fifth or sixth day following injection. Of the 2,175 partially vaccinated subjects, 33 cases of dysentery occurred during the following four days, the percentage being higher in unvaccinated individuals. The morbidity rate in vaccination was 16:1000; among unvaccinated individuals, the morbidity rate was 228:1000. A new and recent test was made in an important group affected by a serious epidemic due to Flexner's bacillus. The polyvalent vaccine was administered in some cases infected with Shiga's bacillus. This vaccine contains 2 billions bacilli per 1 c.c. and is prepared with 8 strains of Shiga, 5 strains of Flexner, 1 of Strong and 3 of Hiss. The monovalent vaccine prepared for each of these bacilli contains one billion per 1 c.c. This polyvalent vaccine acted more effectively than before. The morbidity rate in vaccination was 8.14 per 1000; the mortality was zero. Morbidity and mortality rates among the unvaccinated were, respectively, 70.57 and 1.56, per 1000. For vaccinated cases, the duration was brief (2 to 3 days), or moderate (7 to 9 days). During the first five days following vaccination, simple and transitory diarrhea occurred at the rate of 1.01%. The patient is not sensitized during the period of antibody preparation. In an epidemic, the infecting bacteria should be determined as early as possible, in order to indicate the vaccine most effective. Although belonging to the same family, bacilli of the Shiga, Flexner-Strong and Hiss types are specifically pathogenic. If the type present is not determined, the polyvalent vaccine may be used, but exact determination and use of the appropriate monovalent vaccine are far preferable.

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**Comparative Experiments in the Formation of Antibodies in Gonorrhea.**

*Hermann Fey, Ztschr. f. Immunitätsf. u. exper. Ther., 33:178, Jena, Nov. 18, 1921.*

It was attempted to determine the conduct of gonococcus serum to as many strains of gonococci as possible. A number of gonococcus serums were examined as to agglutination, formation of complement and precipitates, many strains of gonococci being used with each. The serums were from patients who had had the disease for years and in whom it had resisted all forms of treatment. Thirty-three of the serums were examined for agglutination. Suitable dilution of a mixture of 0.5 c.c. of the suspensions of gonococci used as vaccines with 1 c.c. of the serum in question was made and kept for ten hours with a control mixture of Na Cl solution. The cultures used for the suspension were twenty-four hour old (incubator time), were killed with a 0.5% carbolic acid solution; 1 c.c. contained 100 million bacteria. Parallel mixtures were made for agglutination with normal serum and with live cultures. The latter showed a marked tendency to clumping so that it seemed more advantageous to employ dead cultures. By far the greatest number of the serums produced agglutination. These serums reacted differently with different strains of bacteria.

Further experiments were made to determine whether the different strains showed differences in the degree of complement deviation, and whether there was any relation between the complement deviation and agglutination in the sense of the presence of a particularly strong deviation with those strains which were agglutinated by the serum in ques-

tion. The extract of the strains were used in the determination of this latter question. Extracts of pure cultures of gonococci served as antigens. The specificity was found greater with agglutination than with the reaction of complement fixation. The serums which contained a strong complement combining substance showed a tendency to react with all strains, a feature which was less marked in the agglutination test. It is therefore not enough to perform a complement reaction alone, but it may be used in conjunction with agglutination in the determination of suitable strains.

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**Action of Staphylococcal Lysin on the Red Cells of the Goat.**

*L. Walbum, Compt. rend. Soc. de biol., 85:1205, Paris, Dec. 17, 1921.*

Little or no hemolysis occurs at 37° C. and only if there is a large excess of lysin. It takes place during subsequent cooling. The effect depends on the period of incubation at 37°. After four to five hours there is no hemolysis. The cooling temperature was also examined, the mixtures being brought to 20°, 15°, 10° and 0°. The rapidity of the hemolysis is found to correspond to the rapidity with which the temperature is lowered, and the degree of hemolysis is greater in proportion as the point to which the mixture is cooled is low. In making comparative studies of this kind, it is not enough to maintain only the same duration of incubation at 37°. The temperature to which the mixtures are cooled should also be uniform to make the conditions comparable.

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**The Presence and Value of Antibodies in Antituberculosis Vaccination.**

*G. Martinotti, Riv. crit. di clin. med., 22:385, Florence, Nov. 25, 1921.*

Immunization consists in rendering the elements of the body resistant to the attacks of tuberculosis bacilli so that their action is frustrated, rather than in the appearance of bodies especially capable of destroying the tubercle bacilli or of neutralizing their products. In immunization against tuberculosis, the attempt is not to kill the bacilli but to render them harmless by reinforcing the resistance of the body-elements so that they become inaccessible to the aggressions of tubercle bacilli. The argument for use of the author's vaccine should not however be broadened to enter the general field of protein-therapy, for even if it owes its properties to a protein, it is one with a strictly specific action. The thermic reaction is of great importance. It may be severe, slight, or absent. It may be considered the expression of the effort which the organism makes under the vaccine stimulus to put itself into conditions of defense against infection. The phenomenon of antituberculosis immunization is very complex; it originates from cellular activity of which the antibodies (when they exist) are perhaps a manifestation, an activity which can be stimulated by certain substances (vaccines). The author could demonstrate that he proved the value of his vaccine long before the presence of antibodies was demonstrated. The fundamental difference between the author's vaccine and that of Maragliano is a proof of the independence of the former's researches. Martinotti uses a progressive immunization, by many very small injections, while Maragliano uses only one. The two vaccines have nothing in common.

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**Reactions of Leukocytes Following Inoculation with Tubercle Bacilli.**

*M. Vagliano, Compt. rend. Soc. de biol., 85:1130, Paris, Dec. 17, 1921.*

Living and dead bacilli, both of human and bovine origin, were injected into rabbits by the intravenous, intratracheal, subcutaneous and intradermal routes. The fixation reaction with Besredka's antigen was made, to determine any relation between the reactions of the leukocytes and the fixing properties of blood serum. Within a few days after inoculation of dead bacilli, the leukocytes were considerably increased. The increase usually persisted for thirty or forty days. Injection of living bacilli was also followed by an increase. The increase was maintained at a level for ten to twenty days, great variations then ensued and the count became again normal after two or three months. Sensitized dead bacilli produced no change in the count. After inoculation with sensitized living bacilli, the count remained normal for about forty days, then progressively increased. Sensitized dead and living bacilli produced a well marked leukopenia, lasting only twenty-four hours. Some variation in the proportions was produced by the inoculation. Dead bacilli lowered the mononuclears in twenty-four to seventy-two hours. Between the ninth and twelfth days, the proportion of mononuclears was raised for a variable time. The fixation reaction became positive about the twelfth day. Living bacilli produced irregular variations in the mononuclear count. The primary drop during the first twenty-four hours was not constant. Eosinophils were not always increased. Basophils are invariably increased, especially by the living bacilli. In a fresh series of rabbits, injecting the organism produced no change whatever in the leukocyte count.

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**Vaccine Immunity.**

*Kunio Sato, Ztschr. f. Immunitätsf. u. exper. Ther., 32:481, Jena, Oct. 20, 1921.*

As it is no longer possible to ascribe to the cornea a special immunity to vaccine, Sato endeavored to establish experimentally the relation between skin and cornea immunity, the behavior of the antivirulent constituents of the serum with reference to the degree and duration of their activity, the influence of heredity, and of revaccination and its influence upon the antibody content of the blood. The experiments were undertaken with ordinary glycerinized lymph, to which was added physiologic salt solution diluted to 1/50. After settling for two hours, 0.2 c.c. of the clear upper layer was added to 0.2 c.c. of the diluted serum, and kept in the incubator for two hours at 37°. A rabbit's cornea was then inoculated with this mixture. Determination of the virulence titer of the serum was attempted with dilutions of 1/10, 1/20, 1/50, 1/100 and 1/200. For purposes of control a mixture of 0.2 c.c. of physiologic salt solution was used.

The protocols indicate that, beginning on the seventh day and continuing for months, a skin infection protects against a subsequent cornea infection; punctiform vaccination produces complete immunity of the rabbit cornea. Subcutaneous vaccination can also produce skin immunity, but only incomplete immunity of the cornea. As far as the

influence of general immunity upon the cornea is concerned, the experiments show that immunity produced by a skin vaccination also protects the cornea, but the immunity of the cornea varies in degree. It can be complete, so that a separate inoculation of the cornea may react weakly and slowly. The degree of general immunity (skin immunity) bears an important relation to immunity of the cornea. Cutaneous vaccination produces greater immunity of the cornea than does subcutaneous.

It was established that vaccination of the cornea can also produce general immunity. The success of this depends upon the degree of reaction. Immunity is strong if it follows upon bilateral keratitis; it is weaker after unilateral keratitis. Skin immunity is weaker and produced much later than immunity of the cornea after a vaccination of the latter. It is difficult to immunize the second cornea, if only one was inoculated. Even in dilutions of 1:100 and 1:200 the serum of inoculated animals kills the organisms of virulent lymph. The experiments show that antibodies play an important part in vaccine immunity and that Prowacek's theory of small-pox vaccination cannot be maintained. Revaccination, even though it does not produce any reaction, is as effective as successful primary vaccination, so far as the production of antibodies in the serum is concerned. Revaccination produces increased immunity even if no change can be detected on the skin. It is possible that in the human being revaccination also produces an increase of antibodies and increased immunity, without the formation of pustules.

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**Practical Method for Procuring Cow-Pox Vaccine Low in Bacterial Count.**

*H. A. Gins, Deutsch. med. Wchnschr., 47:1362, Berlin, Nov. 10, 1921.*

In order to produce in a short time a lymph containing practically no bacteria, the author makes use of carbolic acid. According to Lentz, the latter is relatively harmless toward the vaccine virus. A certain percentage of phenol was not added to the prepared lymph, as is customary in Japan, but the acid was added to the raw material making transient action of the carbolic acid possible.

The method is practically the following: The raw material is shaken up in the machine with at least 5 times its weight of carbolic acid. It is then shaken up in a large bottle and washed with sterile salt solution at the same time, until a phenol reaction with chlorid of iron is no longer produced. It is then filtered through a fine wire sieve and the original weight of the raw material restored (10-15% is lost). It is prepared for titration with double its weight in salt solution and glycerin. As the 40% concentration of glycerin easily precipitates, 2:1,000 agar is added to the salt solution.

This lymph is ready in twenty-four hours and is highly virulent. It can be used for vaccination, three to five days after taking it from the calf, while the glycerin-lymph, after the old method of procedure, had to be preserved for three to four weeks in 60% glycerin. The action of the phenol, lasting three hours, is much more harmless than the action of the glycerin. This is proved by experiment. The results of all public vaccinations in Berlin and the surrounding territory in 1920 were just as good as before; the reactions were slightly greater.

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The bacteriological examinations gave a favorable result. The bacteriological control before delivery and the examination of the virulence in the animals precludes the possibility of any injury by this very powerful lymph.

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**The Practical Application of Diphtherin Cattle Serum. (A Reply to the Work of R. Kraus, Bonorino Cuenca and A. Sordelli).**

*R. Bicling, Münch. med. Wchnschr., 68:1397, Oct. 28, 1921.*

Kraus, Cuenca and Sordelli reported upon the production of an antitoxic serum for diphtheria and tetanus intoxication in cattle. These authors have evidently forgotten that in Germany, since the year 1912, a diphtheria serum has been used, which is prepared from cattle and tested according to Ehrlich's method. It was manufactured in coöperation with the works of von Pirquet and Rimpau. Its application was advised as follows: once a small dose for the prophylactic serum treatment, to be followed later with curative inoculations with the very effective horse serum, i. e., horse-diphtheria serum; then in large doses for the curative treatment of persons previously treated with horse serum.

The demand for diphtheria cattle serum for curative purposes is very slight in Germany, because even with the use of the 250-ply anti-toxin, for the injection of the same amount of antitoxin units, double as much serum is required as with the use of the highly valuable horse serum.

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**Production of Diphtheritic Toxin.**

*H. Davide and G. Dernby, Compt. rend. Soc. de biol., 85:1177, Paris, Dec. 17, 1921.*

Previous reports have indicated the relations existing between growth of the bacilli, and consequently toxin production, and the reaction (hydrogen ion concentration) of the medium. Toxin production is diminished by alkalinity higher than pH 8.3 Previous experiments indicate that good toxin should be produced in a bouillon acted upon by trypsin. The authors have tried out the plan, especially with reference to the action of hydrogen ions. The bouillon is prepared as follows: mix 6 kg. veal with 12 liters of water heated to 35°; add 10 gm. yeast; macerate in the incubator for four hours; add NaOH to give alkalinity of 6.5 to 7 pH; add 3 gm. trypsin; incubate for about twelve hours, then maintain at 80° for two hours and filter through bolting cloth. Place the resulting bouillon in the refrigerator for some hours, to permit removal of the fat. When the fat has been carefully removed, heat and add 1.5% peptone, 0.4% NaCl and NaOH to give a reaction of 7.1 pH. Filter and sterilize for twenty minutes at 110°. For studying the effects produced by various reactions, the latter have been maintained constant by adding phosphates. Ten test-tubes, each containing 10 c.c. of bouillon, received fifth-normal solution of  $\text{KH}_2\text{PO}_4$  and  $\text{Na}_2\text{H PO}_4$ , decinormal NaOH, and water, to make the contents of each tube 12 c.c. The reaction was determined after sterilization and the tubes were then inoculated with diphtheria bacilli. The results are tabulated; 250 gm. guinea-pigs were used to test the toxin. Maximum toxicity occurred the sixth and seventh days

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after inoculating the tubes. It began to diminish on the eighth day, when the pH reaction had reached 8.4, and continued to grow less as the alkalinity increased. The maximum toxicity was high, the minimum fatal dose being 0.0005 c.c. If the initial reaction of the bouillon is only faintly alkaline (pH of 6.9 to 7.2), the reaction does not affect the toxin until somewhat more than a week. If the initial pH is 7.3 to 7.7, the critical point arrives sooner. For wholesale preparations, the best results were obtained with an initial pH of 7.1 to 7.2. The cultures were removed from the incubator before the pH reaction exceeded about 8.2, which occurred on the sixth or seventh day after inoculation. The toxin thus produced was very strong and did not vary much. The production is more rapid than that obtainable with yeast alone.

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**The Action of Leukocytes and Brain Tissue on Diphtheria and Tetanus Toxins.**

*Augustus B. Wadsworth and R. Vories, J. Immunol., 6:413, Nov., 1921.*

In any study of the bacterial poisons on the leukocytes it is important to determine the chemical or physical reactions, if any, that take place between the leukocyte and the known bacterial toxins such as diphtheria and tetanus toxins. Since the chemical or physical changes in these toxins are indicated and can only be measured by determining changes in the toxic effects they induce in susceptible animals, experiments were performed to discover any loss of toxicity in mixtures of diphtheria toxin and leukocytes such as Wassermann and Takaki demonstrated with mixture of tetanus and brain tissue. Two tables show tests which demonstrate antitoxic potency of leukocytes for diphtheria toxin. It was found that neither the leukocytes of the dog nor those of the guinea-pig neutralize or combine with diphtheria or tetanus toxin. Although brain tissue combines with and neutralizes tetanus toxin, it has no influence on diphtheria toxin.

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**The Reaction of the Rat to Diphtheria Toxin.**

*Arthur F. Coca, Ernest F. Russell and William H. Baughman, J. Immunol., 6:387, Nov., 1921.*

The rat is not absolutely immune to diphtheria toxin: although it usually survives the injection of 1,000 minimal lethal doses (for the guinea-pig) it regularly succumbs to 4,000 such units. The rat is capable of the production of antitoxin upon the repeated injection of diphtheria toxin. The resistance of the rat to diphtheria toxin is not due to the presence of normal antitoxin, but to the property of the cells of preventing the toxin from entering them or attaching itself to them. In the preliminary experiments the first difficulty met with was in the performance of the intravenous injection. By the Shick method they were unable to control the depth of the injection. It was found that Zingher's method, hitherto undescribed or published, insured a truly superficial site of injection. The method is shown in an illustration and is performed by taking up a loose fold of the shaved skin over the forefinger, the needle is inserted superficially near the free border of the fold. The injection of 0.1 c.c. of fluid in this situation always results in the formation of a tense vesicular swelling with a sharply de-

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fined base. Tables show the results of the preliminary test of the toxicity of the toxin with the use of the Roemer method. Constant results can only be obtained with this technic if the larger guinea-pigs are employed.

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**Production of Tetanus Toxin.**

*K. Dernby and B. Allander, Compt. rend. Soc. de biol., 85:1181, Paris, Dec. 17, 1921.*

It is not easy to produce a uniformly good tetanus toxin. The principal factors influencing the result are the specific character of the tetanus bacillus; the composition of the culture medium, especially with reference to nitrogen compounds; variable quantities of accessory substances, such as sugars or salts; substances known as vitamins; metallic catalyzers; and the chemical reaction of the medium. The present report refers to the last factor. English and Dutch bacilli were used, since these produce toxin even aerobically. The reaction must be considered with regard both to growth of the bacilli and to stability of the resulting toxin. For bacillary growth, the pH limits are between 5 and 8.5; the optimum is 7 to 7.6. For stability, the limits are between 5 and 8.8, the optimum being 6 to 7. Destruction of toxin is instantaneous, complete and irreversible in the acid zone, slower in the alkaline zone. Theoretically, the bouillon should not be toxic if the final reaction is below a pH of 6. For making large quantities of strong toxin, suitable for preparing antitetanic serum, the final reaction should be a pH of 7 or more. The method recently adopted is indicated as follows: To bouillon, prepared from fresh meat and lightly sterilized, 0.1% of glucose is added and the pH is brought to 8. The inoculated flasks are titrated at the end of two days. If the reaction is acid, normal NaOH is added to produce a pH alkalinity of 7.5 to 8. The resulting toxins are excellent. Fatal tetanus in mice is produced in less than twenty-four hours by 0.0001 c.c.

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**Intrapulmonary Injection of Serum.**

*P. Mauriac, Pauzat and L. Servantie, Compt. rend. Soc. de biol., 85:919, Paris, Nov. 17, 1921.*

Several good results, obtained clinically in pneumococcic infection, together with the experiments of Sloboziano, suggested further study on this subject. Injections were made in 4 dogs, another animal being used as a control. Injections of antipneumococcic serum varied from 8 to 20 c.c. Sites were: lower lobe, right lung; lower lobe, right lung and pleura; lower lobe, right lung; both lungs (10 c.c. each). No distant lesions were produced; small hemorrhages due to the experimental wounds were present. The animals appeared to suffer no inconvenience, except, in 1, slight transitory dyspnea. Infarct and congestion did not result.

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**Effective Period of Antivenenes.**

*B. Houssay and J. Negrete, Compt. rend. Soc. de biol., 85:1002, Paris, Nov. 26, 1921.*

Deterioration depends on the principle that the quantity of anti-toxin is a function of the square of the quantity of venom neutralized.

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The initial antitoxic value having been measured, that of tubes supposedly no longer useful after thirteen to twenty-three months was also determined. Strong serums, while remaining effective, lose proportionally more activity than weak serums. Losses range from zero to 67% of the initial activity in periods of thirteen to twenty months; but at the end of four years, activity was still very appreciable. It is not necessary to reject old serums, however desirable it may be to use serums freshly prepared. Appearance is not a safe guide, for turbid serums may have preserved their activity better than clear serums. One such serum was examined when twenty months old.

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**Neutralization of Venoms by Antivenenes.**

*B. Houssay and J. Negrete, Compt. rend. Soc. de biol., 85:999, Paris, Nov. 26, 1921.*

Titration of antivenom serums in South America is done by a modified V. Brazil process. To tubes containing each 1 c.c. serum, variable quantities of venom are added, the volumes being made up to 2 c.c. with saline solution. After an hour of contact at 37°, injections are made into the axillary vein of pigeons. The tube corresponding to the first pigeon which survives twenty-four hours indicates the quantity of venom neutralized by 1 c.c. serum. At Buenos Aires, both anti-Lachesis alternatus and anti-Crotalus terrificus values are titrated, the serum being polyclonal. If the neutralizing capacity of different doses of serum be titrated (0.1 c.c. to 1 c.c.), the neutralization is more active as the serum is more dilute. The quantity in milligrams of venom neutralized is a function of the square root of serum concentration in tenths of a cubic centimeter per 2 c.c. Thus, if 1 c.c. serum neutralizes 3.3 mg. venom of *L. alternatus*, 0.1 c.c. will neutralize 1 mg. If the quantity neutralized by 1 c.c. be taken as 1, then 0.75 c.c. will neutralize 0.83 c.c.; 0.7 c.c. will neutralize 0.80; 0.5 c.c., 0.68; 0.4 c.c., 0.606; . . . . 0.1 c.c., 0.3. The results vary if the same titer is used on little birds called "mixtos" (*Sicalis arvensis* or *S. luteola*). Serum and venom are combined as before, 1 c.c. only being injected into the pectoral muscles. These birds show, more clearly than pigeons, that the quantity of venom neutralized is a function of the root 1.52 of the concentration. This result has been determined several times for *L. alternatus* and once for *C. terrificus*. If 1 c.c. neutralizes 1 mg., 0.75 c.c. will neutralize 0.82; 0.5 c.c., 0.63; . . . . 0.1 c.c., 0.21. Antivenom globulin (A. Homer's concentration method) neutralizes more directly, the quantity of venom neutralized being a function of the root 1.15 of pseudoglobulin concentration. A mixture "neutral" for one species is not so for another. There may always be free and displaceable toxin and antitoxin, proteins of the animal dissociate an equilibrated toxin-antitoxin. With pigeons as the test animals, the square proportion must be remembered. If 1 c.c. of serum A neutralizes 2 mg., and 1 c.c. of serum B neutralizes 5 mg., 1 volume of A contains 4 parts antitoxin and the same volume of B contains 25 parts. The precipitin of antivenom serums produces periodic alternation of clouding and transparency with increasing doses of venom. For transparency, the quantity of venom approaches the root 1.4 of serum concentration. For anti-proteolytic power, the quantity of venom neutralized is a function of

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the root 1.52 of the concentration. These reactions are colloidal, recalling the "law" of Schütz and Borissow. The toxin-antitoxin reaction is probably adsorption, which is nearly or wholly irreversible.

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**Anaphylatoxin and Anaphylaxis. XII. Studies on the Chemistry of the Blood.**

*W. M. German, J. Infect. Dis., 30:107, Jan., 1922.*

The phenomenon of anaphylaxis has usually been explained on the basis of observations on the nature of the antigen and its biochemical possibilities when injected, it being assumed that the antigen was the source of the poison. More recently, however, it has been suggested that the serum or tissues of the body are the source of the toxin responsible for the anaphylaxis. This series of experiments was carried out to determine the effect, if any, produced on the alkaline reserve in the process of poison production, and whether or not acidosis has any bearing on anaphylatoxin production or anaphylaxis. With the Van Slyke plasma bicarbonate method it was found that no demonstrable disturbance in the alkaline reserve occurred in the production of anaphylatoxin in vitro in either serum or plasma. Microdeterminations of blood ammonia also showed no variations in this constituent in anaphylotoxic serums as compared with normal serums. In experimental anaphylaxis, specific or nonspecific, no disturbance in the alkaline reserve and no variations in the blood ammonia could be demonstrated. The conclusion is, therefore, that the alkaline reserve is not involved in any demonstrable manner in the phenomenon of anaphylatoxin production and anaphylaxis.

These results are corroborative of those obtained in the study of amino nitrogen in relation to anaphylatoxin, and the general conclusion may be drawn that anaphylatoxin production is not accompanied by changes in amino nitrogen, in blood ammonia, or in the alkaline reserve.

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**The Effect of the Roentgen Rays and Mustard Gas. (Dichloroethyl-Sulphid) on Active Anaphylaxis in the Guinea-Pig.**

*H. J. Corper, Louisa T. Black and Mary Moore, J. Infect. Dis., 30:50, Jan., 1922.*

There was no appreciable ameliorating influence on the reaction resulting from the second injection of a maximum nonlethal dose of Roentgen ray seven days before or coincident with the sensitizing injection of egg white or normal horse serum, or seven days before or with a second injection. Repeated moderate Roentgen ray treatments, sufficient to maintain a low level of the peripheral circulating leukocytes, about 2,000 leukocytes per cm., throughout the incubation period, or very small repeated treatments not noticeably affecting the number of peripheral circulating leukocytes, also had no appreciable ameliorating effect on the severity of the anaphylactic reaction. A slight increase in the severity of the reaction was noted, however, when the Roentgen ray had exerted a profound influence on the hematopoietic system as indicated by the reduction in the number of leukocytes. This result may be due to the intoxication with the Roentgen ray coincidentally with the anaphylactic reaction.

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Subcutaneous injections of mustard-gas in maximum nonlethal doses given seven days before or coincident with the sensitizing injection of egg-white or normal horse serum, or seven days before or with the second injection, were without appreciable influence on the reaction resulting from the second injection of these proteins. Repeated small or medium doses administered throughout the incubation period, being initiated a few days before the first protein injection, also were without appreciable effect.

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**Sapo-Proteose Shock.**

*C. Achard and E. Feuillié, Compt. rend. Soc. de biol., 85:899, Nov. 17, 1921.*

Processes with ether and lime water have been devised especially for demonstrating intracellular union of proteoses with lipoids, fats, fatty acids and soaps. The rabbit was selected for experiments *in vivo*. Intravenous injection of soaps produces disturbances. The authors first found that intravenous injection of 0.05 gm. per 1 kg. body-weight (in rabbits) caused no disturbance. Experiments were then made with 0.04 gm. per 1 kg. Solutions of the same titer were prepared: sodium oleate and Witte's peptone, 0.04 gm. per every 2 c.c. of a 9:1,000 solution sodium chlorid. The solutions were boiled and filtered; the oleate must be neutral and contain no free soda. The oleate used was pasty, resembling yellow wax; the hot, filtered solution should be slightly opalescent. The syringe should be warmed, to avoid immediate death by embolus. Twenty-six rabbits were used, their total weight being 3,400 gm. A 3-kg. rabbit received successively, 6 c.c. of each solution, at an interval of five minutes, the order of using the solutions being varied and giving different results. First injection of Witte's peptone produced polypnea; hemoglobinuria in less than two hours; urine was reddish and urination premature (in fifteen to thirty minutes), as if due to a renovesical reflex; respirations became tranquil in two or three hours after injection; the animal ate; the urine was abundant with no repetition of hemoglobinuria; survival, with normal appearance. First injection of sodium oleate produced: polypnea; no urination; molasses-like fecal discharge, sometimes glairy diarrhea; death in fifteen minutes to forty-eight hours after the double injection, anuria persisting to the end; the animal did not eat; three to six minutes before death, there were violent convulsions. One out of 7 rabbits survived after a urinary crisis following forty-eight hours of fasting and anuria. The contrast between these effects is more strikingly shown by using the same dose of peptone, the latter being exhausted in alcohol and kept for twenty-four hours in Kumagawa's apparatus; no change was made in the sodium oleate. First injection of Witte's peptone produced: intense hemoglobinuria; normal recovery in two to three hours. First injection of sodium oleate: Before the injection was finished, the animal turned upon its flank; dyspnea, not polypnea; death in three to six minutes. *In vitro*, an excess of soap prolongs suspension of the sapoproteose complex; excess of albumoses (peptone) rapidly produces precipitation. No full explanation is attempted. Special shock must exist; neither solution, given alone, produces any pathological manifestation.

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**Leukocytic Variations in Peptone Shock Resulting from Modified Excitability of the Organole vegetative Nervous System.**

*L. Garrelon and D. Santenoise, Compt. rend. Soc. de biol., 85:903, Paris, Nov. 17, 1921.*

Digestive leukopenia appeared to vary according to variations in irritability of the neurovegetative system. Tests were made, hemoclastic shock being induced by intravenous injection of peptone, and parasympathetic (opposite) variations by pilocarpin and atropin. Injection was delayed after chloralose anesthesia long enough to permit the slight leukopenia induced by the anesthetic to disappear, which required from an hour to an hour and a quarter. Five to 6 mg. per kilo body-weight sufficed to induce the leukopenic (hemoclastic) shock. The parasympathetic was rendered hyperirritable by injection of 1 cg. pilocarpin, the leukopenia being pronounced, as usual (from normal of 5,600, decline to 3,600, leukocytes) and accompanied by intense peripheral vasoconstriction. The parasympathetic was rendered hypo-irritable by injection of 1 mg. atropin, leukopenia being inhibited (from 5,400, rise to 6,600, leukocytes) and not followed by hypotension. The neurovegetative system, therefore, probably intervenes in peptone shock. The effects of peptone-injection on the oculocardiac reflex confirm these findings; pressure before injection gave a pulse-rate of 95 (vagotonus); forty-five minutes after injection, rate of 110; seventy-five minutes after injection, rate of 138 (hypovagotonus). The oculocardiac reflex is diminished for some time after a test meal. Possibly there is a relation between modified parasympathetic irritability and the immunizing effect of a prior injection of peptone.

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**Parafocal Pharmacodynamic Allergy According to the Method of von Gröer and Hecht.**

*A. F. Hecht, Wien. klin. Wchnschr., 34:580, Dec. 1, 1921.*

The cutaneous reaction was examined as to the effect of a 1% morphin solution and a 1% ketone base solution applied within the diseased area of skin and in the periphery of these areas. This followed the observation of a distinct, anemic zone, around the edge of hyperemic efflorescences, as in measles and other exanthems. These anemic areas are again surrounded by a teleangiectasis. A further reason for the experiments are the observations of Koch and Schiller as to differences in the focal parafocal reactions in the tuberculous, inflammatory skin reactions in the use of Pirquet's test. The results are summarized as follows: (1) Pallor and exudation reactions are reduced within the area of hyperemia of the skin. This reduction is noticeable beyond the areas of skin which are involved and changed. (2) There are often contrary changes in the skin reaction in the presence of efflorescences. This condition is suggested by the presence of the pale area. (3) Intracutaneous and cutaneous tuberculin reactions show a variable parafocal manifestation as compared with Pirquet's cutaneous reaction. This may be explained as changed tendency of the reaction or one that is not specific. The specific parafocal reaction which is a distribution of the antibodies in the region of the tuberculous infiltrate cannot, therefore, appear distinctly. (4) The diminution of the tendency to exudate

formation may be demonstrated as far as 25 mm. away from the inflammatory infiltrate. This throws some light on the possible value of the so-called counterirritation.

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**Problems in Serology of Carcinoma.**

*N. Waterman, Nederl. Tijdschr. v. Geneesk., 65:2388, Haarlem, Nov. 12, 1921.*

The process of malignant tumor growth affects the entire organism. Without a knowledge of the different reactions of the organism before and after the development of the tumor no progress in the biologic study of tumors can be made. Therefore, it is quite logical that changes should be looked for in the blood. This makes possible the development of an improved humoral pathology in harmony with the theory of cellular pathology. In the study of this disease, for which no parasitic agent can be presumed, the empiric methods borrowed from the serology of the infectious diseases cannot be directly applied. A study of immunity must be combined with that of physical chemistry. The lack of such systematic research helps to explain why so little is known about the most elementary qualities of serum, plasma and blood in the growth of carcinoma. To be sure, certain serodiagnostic methods exist, all of which are interesting. Practically, only the miostagmin reaction is of importance, at least when the practical reliability of the method can be improved. This reaction also has theoretic importance in that it has introduced the notion of surface tension in the pathology of tumors.

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**The Influence of Temperature upon the Agglutination of the Red Blood-Corpuscles.**

*Fredrik Jervell, J. Immunol., 6:445, Nov., 1921.*

A number of experiments were carried out in order to find out whether the agglutination of the corpuscles was strongest at 8° or 37°. Tables show the set ups and the results of all the tests. Some of the sets were run in the incubator and others in the ice chest. Agglutination in the ice-chest was more marked, due to more complete adsorption of agglutinin at low than at high temperature. When brought into higher temperatures after adsorption at 8° the corpuscles again lose part of the agglutinin. Another experiment was made to find the amount of blood-corpuscles required to adsorb a certain amount of agglutinin at different temperatures. These indicate that maximal adsorption of agglutinin is different at different temperatures and more nearly complete at the low than at the high temperatures. When the adsorption had been carried out at a low temperature and the corpuscles after that were placed at a higher temperature, they could retain only the quantity of agglutinin corresponding to the maximum for the respective temperature and accordingly lost agglutinin until this maximum is reached.

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**Physiological Agglutination of Dysentery Bacteria I.**

*O. Hausherr, Cntrbl. f. Bakteriol., etc., 87:95, Jena, Sept. 15, 1921.*

After a critical review of the literature the writer admits the specific character of agglutination of dysentery bacteria by human serum.  
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The term "physiologic agglutination" is given to the flocculation of dysentery bacteria Y by the serum of parturient women (first described by Loewenthal and Bertkau), in order to distinguish it from the specific agglutination produced by cured dysentery. The writer, working with material of his own, confirms the existence of this phenomenon, the conspicuousness of it varying with different species. He noticed it also when using dysentery bacteria of the Flexner type, while typhoid, Shiga-Kruse and cholera bacteria did not give uniform results. Extraction with ether does not remove from the serum of gravid women the property of agglutinating Y-bacteria.

Therefore, the writer comes to the conclusion that physiological agglutination does not depend upon the lipoid contents of the serum.

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**The Normal Limit of Agglutination for *Bacillus Dysenteriae* (Flexner) and the Sensitiveness of Suspensions.**

*A. D. Gardner, Lancet, 2:1269, London, Dec. 17, 1921.*

In an article on the Etiology of Bacillary Dysentery (*Lancet*, July 30), Dawson and Moodie state that with the Oxford antigen the first trace of agglutinins appeared at the end of the sixth week, and the agglutinins had disappeared at the end of the fourteenth week; while with Dudgeon's antigen, agglutination began to appear at about the beginning of the fourth week, and had disappeared at the end of the fourteenth week. Maximum agglutination was obtained with Oxford antigen between the eighth and tenth week, and with Dudgeon's antigen in the seventh week. As this paper would imply that Dudgeon's antigen was a more serviceable material than the standard cultures issued from Oxford, the writer secured a sample of antigen made in the same way and with the same culture as that used by Dawson and Moodie. The strain of Flexner bacillus used in its manufacture is known as Flexner Gallipoli, of which a living culture was obtained. The antigen was apparently a saline suspension of the bacillus, with a preservative added. Its density was somewhat about three times greater than that of "standard" dysentery cultures. Tested with standard dysentery Flexner (V) serum, it gave first-rate flocculation up to a dilution between two or three times greater than was given by the standard culture (Flexner V 12) used in comparison. Dudgeon's antigen thus proved to be a suspension of great sensitiveness. At the same time it betrayed no tendency to spontaneous flocculation. The "Flexner Gallipoli" was found to be of the same group as the stock Flexner "V" of the Standard Laboratories. It remained to consider whether the use of this strain for serodiagnostic suspensions (e. g., for the manufacture of standard cultures) would be an improvement on the less sensitive strains such as the Oxford stock Flexner V. Absolutely indispensable for the trustworthy use of any bacillary suspension in serodiagnosis is the determination of the normal limit of agglutination with that particular suspension. This can only be done by testing a large number of normal serums with the suspension itself, or by determining the sensitiveness of the suspension in comparison with another suspension which has been thus tested. A determination of the normal limit of agglutination for a suspension of the bacillus was carried out on over a hundred men and women. Not a single man whose past history was clear of dysentery gave a reading of as much as standard agglutination at a dilution of 1 in 50 with the suspension used.

All subsequent suspensions (standardized cultures) of this type of bacillus have been carefully compared with the original suspension or with one or several suspensions successively standardized, each against a previous one. The superior sensitiveness of Flexner Gallipoli was equally evident whether specific or normal serums were used. Summarizing the findings, just as specific serums give a much higher titer with Flexner Gallipoli suspensions than with Oxford standard cultures, so do normal serums. Owing to the presence of "Flexner" agglutinins in normal serums, highly sensitive suspensions are, for the purpose of clinical diagnosis, of no greater value than those less sensitive.

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**Johne's Disease and Its Detection.**

*B. A. Beach and E. G. Hastings, J. Infect. Dis., 30:68, Jan., 1922.*

Tests were carried out on entire herds of cattle to determine whether Johne's disease (chronic dysentery, paratuberculosis) can be eradicated by the use of johnin, a product from the specific organism, which is comparable to tuberculin in the manner of its preparation, in the mode of its administration, and in its action on the infected animals. The constitutional reactions are sometimes very severe. The results obtained indicate the possibility that the disease can be eliminated by the use of johnin. These results were confirmed by macroscopic and microscopic examinations of the tissues, and in a few instances by second tests on reacting animals. Acid-fast bacilli were found in 29 of the 30 animals which reacted. One herd was tested 8 times in four years, reactors being obtained at each test except the last.

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**Serological and Morphological Characteristics of the Pneumococcus: An Analysis of Organisms Isolated from Seventy-seven Cases of Pneumococcal Infection.**

*A. L. Urquhart, Lancet, 2:1313, London, Dec. 24, 1921.*

Comparison has been made of Lister's standard strains of pneumococci, from cases of lobar pneumonia and their homologous antisera, from the South Africa Institute for Medical Research, with strains of pneumococci, present in Great Britain, isolated from cases of lobar pneumonia, and from cases of pneumococcal infection other than lobar. Experiments in isolating pneumococci from pus and sputum, studies of the morphologic and cultural characteristics, results of blood culture, investigation of the formation of specific agglutinins and opsonins in the blood-serum of persons suffering from pneumococcal infections, experiments with the serologic reactions of 77 strains of pneumococci isolated from various sources, the Lister results correlated with those of the Rockefeller Institute and other workers by means of Rockefeller anti-pneumococcal serums (full details set forth in tables, etc.), brought out the following facts: From the laboratory methods employed, the pneumococcus presents its most typical appearance in fresh body exudates; bile solubility and the absence of hemolytic activity are almost constant characteristics of the pneumococcus. For the separation of pneumococci in sputum and pus, Dudgeon's method was convenient and satisfactory. The fermentation reactions of the pneumococcus were of no value for the division of the organisms into types. Pneumococcal antibodies corresponding to the type of pneumococcus responsible for

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the infection, though not present in the early stages of the disease, were usually formed in the postcritical blood serum of cases of lobar pneumonia, and in the later stages of some other pneumococcal infections. The pneumococci responsible for lobar pneumonia and other serious pneumococcal infections in this country are similar to those found in America and South Africa. Type IV pneumococci were capable of producing any of the serious infections, due more commonly to types I and II infections.

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**The Reaction of the Blood Serum in Relation to Colloid-Lability in Toxic Conditions, Especially in Active Tuberculosis.**

*Darani Julius, Orvosi hetil., 65:409, Budapest, Nov. 20, 1921.*

There are two principal proteins in the blood, serum globulin and serum albumin. The former is precipitated more easily with certain reagents. The greater the quantity of such easily precipitated albumins, the greater the colloid-lability of the solution discussed.

The author examined the colloid-lability of the blood serum in 450 cases, 115 of which were of tuberculosis. The latter included 22 cases of healed and inactive tuberculosis. There were 190 healthy subjects, 36 of whom were pregnant. The rest were patients with bacterial and nonbacterial diseases. It could be shown in a general way that the colloid-lability of the blood serum increased every time there was formation of toxin and destruction of tissue in the body.

The author added 1.1 c.c. of diluted alcohol to 0.2 c.c. of serum. The test-tubes were well shaken, placed in water bath at 60° C. for twenty minutes and the results were read at room temperature in one, two, three and twenty-four hours after warming in the bath. The author considered a precipitate as a sign of completed reaction, in from one-half to one hour, as 4+; in two hours, as 3+; in three hours, as 3+; in twenty-four hour, as +.

The alcohol was 96% and was diluted with a 2% NaCl solution.

Healthy subjects showed no reaction. Negative or weak reaction after twenty-four hours was obtained in superficial inflammations (cystitis, bronchitis, gastritis, catarrhal, conjunctivitis, urethritis, cholecystitis) and in cholelithiasis. A marked reaction, which appeared in three hours at the latest, was seen in processes which penetrated deeply into the tissues, as in suppurative appendicitis. The reaction was negative in benign, stationary tumors but was strongly positive in progressively disintegrating tumors. The weakening or disappearance of the reaction may be considered as a therapeutic control. It may also be used as a means of making a prognosis. Only a 4+ or 3+ reaction is an indication for the interruption of pregnancy in tuberculosis.

The reaction is especially of value to determine the activity of tuberculosis. The reaction is never absent in active cases and the strength of the reaction runs parallel with the extension of the process, the formation of toxins and degeneration of tissue. The reaction again becomes negative after healing has occurred.

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**Agglutination of the X-Strains.**

*S. Büchner and W. Zorn, Ztschr. f. Immunitätsf. u. exper. Ther., 33:115, Jena, Nov. 18, 1921.*

There is no parallelism between the effects of the patient's serum and the immune serum made by treatment with Weil-Felix bacilli in rabbits. Differences were seen after warming immune and antiserums, after the effect of heat, prolonged standing and addition of chemicals or changed bacteria. The experiments of Weil and Felix with the O and H forms of the "X" bacillus explains the differences between typhus serum and immune serum of rabbits. The agglutination of the O form is always in fine flakes, while that of the H form is agglutinated in coarse flakes. A serum may be obtained from rabbits which have been immunized with O bacilli; this serum will agglutinate only those types of O form of "X" bacillus (X2 especially X19) which have been used in the production of the immunization. The immune serums which were produced with the H form will agglutinate the H form and also the X19 and X2 types. The serum of patients with typhus agglutinates the "X" bacilli in fine flakes. It resembles the pure O serum because, like the latter, it is possible to produce the X19 form by immunization of rabbits. No differences are known between the serum of patients with typhus and the serum of rabbits which have been immunized with the O X 19 form. The same differences are present between the serum of patients with typhus and H immune serum of rabbits as exists between the H and O immune serums of rabbits. Flocculation with the serum of typhus patients is hindered or impossible, if the H form is carefully heated ( $50^{\circ}$ - $56^{\circ}$ ), or is allowed to become cold. This effect is not produced with the immune serum of rabbits. Weil was able to produce agglutinins in the rabbit against X19 by previous treatment with the brain of a guinea-pig which was infected with typhus. He then examined the characteristics of the typhus agglutinins of the rabbit, serum of patients with typhus and the immune serum of rabbits which were previously treated with the X2, O and H forms of the X19 bacillus.

Examination was made of the immune serum of rabbits which were previously treated with the H form of the X19 bacillus. The serum was examined in the fresh state and after heating at  $70^{\circ}$  for one hour. Examination was also made of the O and H form of the X19, H form of the X2 in fresh emulsion and after heating at  $52^{\circ}$  for one hour and after heating at  $100^{\circ}$ . Twenty-four-hour slant agar cultures were used in all instances. The bacterial suspensions were made with salt solutions and 1 drop of this was added to each drop of diluted serum. The emulsion was heated to  $100^{\circ}$  for ten minutes. Conservation of the serum was accomplished by adding 0.1 c.c. of a 5% phenol solution. The serum of typhus patients was also examined in the fresh state and after heating at  $70^{\circ}$  for one hour. The O agglutinins are destroyed by heating the H X19 and the H X2 immune serum of rabbits at  $70^{\circ}$  for one hour. The H agglutinins were weakened by the same process. As a result of this, the author saw agglutination with coarse flakes in bacteria with retained H receptors such as H X19, H X2, H X19, at  $52^{\circ}$ . Heating of the O X19 immune serum of the rabbit (pure O serum and serum of a typhus patient at  $70^{\circ}$  for one hour) resulted in destruction of the O agglutinins, which were the only ones present. Absence of agglutination was the result of this.

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The virus serum of the rabbit reacts like the O X19 rabbit immune serum or the serum of a typhus patient both in the fresh state and after being heated at 70° for one hour. This may mean that O X19 bacilli are present in patients with typhus. These bacilli may be the real antigens which form the antibodies. This would tend to support the supposition that the O X19 bacillus of Weil-Felix is the etiological factor of typhus.

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**The Relation between Bile Salts and Hemolysis in the Blood Stream.**

*Eric Ponder, Brit. J. Exper. Path., 2:289, London, Dec., 1921.*

The normal amount of bile acids produced in man is about 10 gm. a day; but only traces of bile salts are found in the normal urine. Although in the first few days of jaundice, bile salts are absorbed into the blood-stream in increased amount there is no hemoglobinuria present, and there is little bile salt excreted in the urine. Ponder states that the bile salts do not cause hemolysis when in the blood-stream, nor does hemoglobinuria follow their injection. Since the blood is not acid, they do not enter into an absorption compound with the albumins of the serum. The bile salts have colloidal properties and so are excreted with difficulty by the kidney.

Although these conclusions were true when chemically worked out, Ponder carried out similar experiments on the rabbit. Under chloroform the jugular vein was exposed and a cannula inserted. A sample of normal urine was obtained. The urine was collected from the bladder by a tube, and 2 c.c. of a 1:800 solution of sodium taurocholate in saline was injected into the jugular. Both breathing and the heart-beat became slower. The amount of urine excreted became diminished. No hemoglobinuria appeared. In half an hour, when breathing and heart-beat became normal, 2 c.c. of a 1:80 solution of sodium taurocholate in saline was injected intravenously. A similar slight effect in the respirations and heart-beat occurred. The secretion of urine appeared to cease almost completely. Finally in a collection of 1 c.c. of urine, no sign of hemoglobinuria was demonstrated. The rabbit was killed and there was no hemoglobinuria in the serum drawn off. The urine collected after injection of the bile salt was more concentrated than that collected first. On applying the reaction of Pettenkofer, according to Bertrand, there was found to be no bile salts in the normal specimen of urine and only very slight traces in the urine collected after injection of the bile salts.

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**An Antihemolytic Substance Occurring in the Serum of Maia Squinado.**

*J. Cantacuzène, Compt. rend. Soc. de biol., 85:970, Paris, Nov. 26, 1921.*

Previous studies indicated that the blood of maia contains a thermolabile substance increased by vaccination. This substance, adsorbed by sensitized erythrocytes, opposes fixation of complement by the red cells. Its existence is shown by the following method: sensitized sheep's erythrocytes are left in contact with serum of maia for several hours, then centrifuged, washed with isotonic sea-water and emulsified in a volume of isotonic solution equal to that of the serum decanted and (Sec. 1—Page 357)

receiving an addition of alexin. By hypothesis, the red cells should not be hemolyzed. Control red cells, not sensitized, are likewise left in contact with maia serum and subjected to the other processes, being finally sensitized by anti-sheep serum and brought in contact with alexin. The mixtures, left in contact for five hours, were composed of 4 c.c. of 1/20 red cell emulsion and 10 c.c. maia serum. Results were very definite, as follows: Serum of maia (neither normal nor vaccinated) contains no substance capable of preventing sensitization of red cells. In the case of red cells previously sensitized and then subjected to contact with the serum, the conditions are quite different. Inhibition is due, not to saline concentration of the serum, but to an inhibiting substance which becomes fixed to the sensitized red cells, energetically diminishing their ability to fix alexin. This inhibiting substance, present in normal maia, develops abundantly by vaccination, which probably causes extreme slowing of red cell lysis, and permits completer phagocytosis, within the living crustacean. The anti-alexic power develops together with hemolytic capacity, but more rapidly. The inhibiting effect is destroyed by heating maia serum to 57°. Existence of a thermolabile antibody within the normal maia, increased by vaccinating the animal, is thus confirmed.

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**Experiments Showing the Importance of Sequence in Biologic Research. II.**

*Karczag and K. Lajos, Biochem, Ztschr., 122:52, Berlin, Sept. 26. 1921.*

For the experimental proof of the law of sequence, the following experiments were carried out: (1) On the antitryptic power of blood serum on the system (trypsin 1%+casein 2%+blood serum 2%). (2) With the hemolytic system: red blood-corpuscles (0.5 c.c.)+complement (0.5 c.c. diluted in the proportion 1:10)+hemolysin (0.5 c.c. dilution). (3) Animal experiments on the bacteriolytic action of immunizing serum on paratyphoid bacilli in Pfeiffer's experiment (with paratyphoid B serum (1 loop)+guinea-pig). In the first case alteration of the sequence caused an alteration in the antitryptic power. In the case of the hemolytic system, the effect of the previously added hemolysin made itself felt instantly. Therefore, the sensitizing is, in this case, the reaction optimum of a system whose members were arranged in optimal sequence. The sequence optimum and sequence pessimum, therefore, respectively render the conceptions of sensitization and inhibition superfluous. In the experiment on the bacteriolysis of paratyphoid B by the immunizing serum on guinea-pigs (Pfeiffer's test) the sequence optimum signified that the animal overcame the infection, while the sequence pessimum denoted grave illness and death.

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**The Standardization of Suspensions of Red Blood-Cells for Wassermann Tests.**

*Joseph W. Bigger, Lancet, 101:1369, London, Dec. 31, 1921.*

A simple and rapid method of standardizing red blood cell suspension consists of the following steps: (1) A suspension of cells (N. S.) is made which is stronger than the one required. (2) 1.0 c.c. of N. S. is measured accurately with a 1 c.c. pipet into each of six or eight clean, dry test-tubes (a), (b), (c), (d), etc. (3) To (a) add 3.0 c.c. (Sec. 1—Page 358)

of water, to (b) add 4.0 c.c., to (c) add 5.0 c.c., to (d) add 6.0 c.c. (4) The contents of each tube are mixed and coal-gas bubbled through by means of a fine glass tube until the carboxyhemoglobin color is fully developed. A portion of each is transferred to the comparison tube of a Haldane's hemoglobinometer set, and its color compared with that of the standard tube. Some of the dilutions will be found to be dark in color and some too light. Suppose (a) and (b) are too dark and (c) too light. (It is not necessary to wash out and dry the comparison tube after each dilution is tested. It is quite sufficient to empty it, shake it out, and rinse with a small quantity of the next dilution to be tested.) (5) To (e) add 4.5 c.c. of water, mix, pass gas through, and compare. Suppose (e) is too light. (6) To (f) add 4.2 cc. of water, mix, pass gas through, and compare. Suppose (f) is just too dark. (7) To (g) add 4.3 c.c. of water, mix, pass gas through, and compare. Suppose (g) exactly matches the standard tint. It is then evident that 1 c.c. of N. S. plus 4.3 c.c. of water gives a solution containing exactly the same amount of hemoglobin as Haldane's. The amount which the N. S. must be diluted to produce S. S. can now be calculated. In order to save trouble a formula may be used. If  $x$  c.c. is the amount of water necessary to

x-3

add to 1 c.c. to give Haldane's tint, — c.c. of saline must be added to  
4

each 1 c.c. of N. S. to produce S. S. = 4H. In the example given,  $x = 4.3$  c.c., so 0.325 c.c. of saline must be added to each 1 c.c. of N. S., or 13 c.c. to 40 c.c. Since the whole operation of preparing a standard suspension takes about 10 minutes, it does not add unduly to the time necessary to perform a Wassermann test. No difficulty was experienced in color matching.

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**Two Methods of Complement Preservation for the Wassermann Reaction.**

*Karl Klein, Münch. med. Wchnschr., 68:1453, Nov. 11, 1921.*

Hammerschmidt preserves the complement of guinea-pig serum by adding to 4 parts of fresh serum 6 parts of a 10% solution of sodium acetate, and keeping the mixture on ice. Testing this against the hemolytic system of the Wassermann reaction, the author found that the sodium acetate preserved the complement action to a satisfactory degree for about seven days, but that after that time it rapidly diminished. When used in the complete Wassermann test, in 2 cases the sodium acetate mixture showed an increased tendency to negative results after only three days, and in nearly every instance after seven days, while controls with fresh complement gave a 4 plus reaction. That is, when guinea-pig serum and sodium acetate are allowed to stand for a number of days, some development takes place in the mixture which influences hemolytic action independent of complement formation. Since this does not occur when sodium acetate is added to fresh serum, it seems reasonable to attribute the change to bacterial growth. The tendency to spontaneous inhibition which appears in positive serums when used with complement more than a week old, can be explained on the ground of a simple diminution of complement, and in the same way can be explained the fact that negative serums, when used with old complement, tend to inhibit hemolysis and simulate a positive result. The author, therefore,

cannot recommend this method of conservation. Good results were obtained with Mohr's method of freezing with  $\text{CO}_2$ , but this is too costly and too complicated for small laboratories.

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**Scientific and Practical Notes on the Wassermann Reaction.**

*Carlos Martelli, Arch. de cardiol. y hematol., 2:389, Madrid, Nov., 1921.*

There is no very close correspondence between the results obtained by various technicians whose ability is unquestionable. The discrepancies relate principally to 4 factors and depend upon conditions governing these factors. (1) The reaction must be interpreted by studying the results obtained with different antigens. Those prepared from syphilitic liver are usually more sensitive than those derived from guinea-pig's heart, but sometimes the reverse is true. The findings more generally correspond in recent syphilis. Variations are greatest in the chronic and parasyphilitic forms. The difficulty may be largely avoided by testing a given serum with different antigens and averaging the results. The original technic of the Wassermann gives more uniform results. (2) There is no doubt that the reaction is specific, but much depends on the manner of verifying the final conclusion. Syphilis is so widely distributed that the Wassermann is often unexpectedly positive. In order to be sure of his ground, Martelli generally uses 5 or 6 different antigens, rarely 3, and 9 or 10 in doubtful cases. The material should always be fresh and tested. The Wassermann is specific for active or reactivated syphilis, but complement fixation is not, since it may be obtained with guinea-pig's heart, cholesterol, etc., which have no relation to the treponema or to syphilitic tissues. Colloids similar to those of syphilis may probably be produced by other morbid processes, especially those caused by protozoa. A 2+ to 4+ reaction, obtained with 4 or 5 antigens and different methods, is positive proof of syphilis, especially if given by a small quantity of serum. Partial and doubtful reactions may be produced by malaria, leprosy, pneumonia, tuberculosis, cancer, exophthalmic goiter and other conditions. (3) Serums obtained from active, recent and untreated cases give strongly positive reactions in quantities of only 0.01 to 0.02 c.c.; the usual quantity of 0.1 to 0.2 c.c. is quite sufficient to produce the reaction. Where the reaction is negative, partial and doubtful, from 0.4 to 0.5 c.c. of serum may be used. The reason for varying the quantity of serum arises from the fact that the serum globulins or lipoids may vary with the time elapsing after infection, and with the treatment and resistance. The quantity of antibodies is directly proportional to recency of infection and to the absence or insufficiency of treatment. By trying out different quantities of serum, the effects of treatment may be noted. Relatively large quantities (0.4 to 0.5 c.c.) do not disturb the reaction, while the latter is not positive with a non-syphilitic serum. Quantities of 0.6 to 0.9 c.c. are too large; not more than 0.5 c.c. should ever be used. Care should be taken not to convey reagents from one tube to another by liquid remaining on the finger used to close the tube while shaking it. These quantitative conclusions are based on 310 cases. (4) During the course of syphilis, anergic or latent periods occur, during which the Wassermann may be negative. Where the reaction is doubtful for this reason, attempts to secure a positive reaction may be made by using larger quantities of serum (up to 0.5 c.c.).

or special antigens. This technical method is not invariably sure. The biologic method (inducing a positive reaction by specific treatment with arsenicals, mercury or iodids) is very valuable. Intravenous injection of 15 cg. novarsenobenzol is usually satisfactory, or 5 cg. calomel or 6 to 7 cg. mercury biniodid may be used, preferably together with colloidal sulphur. The author's best results were obtained with these methods. Intramuscular injections of novarsen were somewhat less satisfactory and mercurial inunctions yielded the smallest returns. Inunctions should be given by experienced persons in 10 sittings of thirty to forty-five minutes each. Of 565 attempts to obtain a positive reaction in this way, the author was successful in 370 cases (65.46%). Early positive reactions may be obtained in five to ten days after the first period of treatment, or, in delayed cases, in twenty to thirty-five days. For scientific purposes, the reaction should be confirmed in one, two, three, four and five weeks, but for practical results only after the first and fifth weeks.

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**Experiments for Comparing "Official Extracts" for the Wassermann Reaction.**

*Carl Stern, Deutsch. med Wchnschr., 47:1463, Berlin, Dec. 1, 1921.*

Last year a sort of police concession was planned for Wassermann tests. The protest of many experts, however, persuaded the department to yield to the extent that every examiner was obliged to use a municipally tested extract for each examination. The author supervised the control in his clinic, where it is customary to evaluate each extract according to previous tests and in comparison with other, approved ones. Sachs-Georgi and Meinicke tests are also made. The results are controlled by comparison with tests of positive syphilitic serum of varying reaction. Of 574 serums results with extract of clinic and of Frankfort (official extract) tallied in 506 and differed in 68; of the latter, 3 cases were negative with clinic extracts, but positive with Frankfort although without any clinical signs of syphilis, and negative for Sachs-Georgi and Meinicke. Tests with 65 serums were positive with clinic extracts, tallying with clinical reports, Sachs-Georgi and Meinicke, but negative with Frankfort.

The same holds good for the Wassermann reaction as for Roentgen examination; each individual must adapt himself to his own method and weigh pros and cons. Hence it would be wrong to consider the results with the "officially tested extracts" as the sole deciding factor. It cannot be said that the use of such an extract alone should be considered decisive. There is no chemically stable extract. The same serum tested on two successive days may give quite different results. The extract is not the only deciding factor in the Wassermann. The official extracts were not better than those prepared in the clinic.

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**Weak Dilutions of the Cerebrospinal Fluid in the Bordet-Wassermann Reaction Obtained by the Dilution Method.**

*E. Peyre and R. Targowla, Compt. rend. Soc. de biol., 85:1019, Paris, Dec. 3, 1921.*

In the fluids of 180 mental cases, comparison was made of the fixation test as obtained by various methods. The leukocytes and  
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albumin were determined and Guillain's colloidal benzoin reaction was made. The leukocytes were counted in Nageotte's counting chamber, albumin was estimated by Sicard and Cantaboule's rachi-albuminometer and globulins were determined by the carbolic acid test. On the whole, Vernes' technic practically agreed with the dilution method (minimal dilution, 1:10); naturally the 2 notations are not identical. The ordinary Wassermann was a little less sensitive. In certain cases of general paresis during remission, of latent syphilis, undeveloping congenital syphilis and syphilitic meningitis, the fixation reaction was negative, notwithstanding certain clinical evidences. To complete the studies, weaker dilutions (1:5 and 1:2) of the cerebrospinal fluid were employed, by the dilution method, in 8 cases, as follows: 6 during remission of general paresis; congenital lues (mentally defective, epileptic and with a specific lesion of the ear), 1 case; cerebral syphilis, with mental impairment, cured paralysis of the third nerve and epileptiform crises, 1 case. The reaction was positive in all. The dilution method is thus very sensitive. It is positive during remissions in general paresis and when other tests fail. Guillain's reaction was negative in 1 case with variable albumin and constant lymphocytosis. This condition may constitute the only sign of latent syphilis of the nervous system.

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(1e—189)

(1e—189)

**Disappearance of the Substances in Syphilitic Serum, Which React in the Various Tests after Treatment with Formaldehyd.**

*H. Dold, Deutsch. med. Wchnschr., 47:1485, Berlin, Dec. 8, 1921.*

The precipitation of lipoid substances is the principle of syphilitic serologic reactions. Dold attempted to determine whether there were processes of swelling in the formation of the flakes. Formalin withdraws water, hardens tissue and deprives gelatin of the property of swelling up. He added formalin to the extract solution and to the serum before they were brought together and watched for the turbidity reaction, which appears early and microscopically. Addition of formaldehyd to the extract caused it to lose its power to react with syphilitic serum in the characteristic manner. The damaging influence is chiefly on the part of the complement and less of the hemolytic amboceptor. It is possible to follow the turbidity flaking reaction of the author from the time that the extracts and serum are mixed to the conclusion of the test. Swelling processes are a factor in precipitation in general, and in the flaking of the extract-lipoids with syphilitic serum in particular. The addition of formaldehyd, as for purposes of preservation, should therefore be avoided.

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**Action of Formol on Colloidal Solutions Other than Human Serum.**

*Gaté and G. Papacostas, Compt. rend. Soc. de biol., 85:1029, Paris. Dec. 3, 1921.*

The precipitation of albumins in syphilitic serum obtained with formol suggested further study of the relations of the reaction. Solutions of protargol, electrargol, colloidal tin, colloidal gold and peptone, and serums of the guinea-pig, rabbit and horse, were examined. All remained unaltered. The reaction is probably limited to syphilitic serums. Whatever the mechanism of the production of the formol gel.

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the latter may possibly contain substances capable of fixing complement in the Wassermann reaction. Hemolysis was invariably absent in all the examinations made of the gel and coagula obtained from syphilitic serums; this result is due to the antihemolytic action of the formal, as proved by specific test. Solution of this problem is very difficult, if not impossible, for chemical study of the formal-treated serum would so alter its character as to prevent checking the results with the Wassermann.

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**Theoretical and Practical Results of Meinicke's Flocculation Reaction.**

*Walther Jantzen, Ztschr. f. Immunitätsf. u. exper. Ther., 33:156, Jena, Nov. 24, 1921.*

Wassermanns according to the original method were performed at the same time as the examination according to Meinicke. This was done because the Wassermann reaction is negative if there was antisyphilitic treatment shortly before or where little syphilitic antibody had developed. The slightest excess of complement may mar the result in the latter instance. It was also attempted to determine whether antisyphilitic treatment influenced the Wassermann and Meinicke reactions to the same degree. It was impossible to determine the effects of mercury and salvarsan separately as in all cases the combined treatment had been used. The third modification of the Meinicke reaction was used, as the original method is quite complicated and the former is as simple as the Sachs-Georgi reaction. The serums were from patients under treatment as well as from those not under treatment, and included all stages of syphilis.

Results: The D.M. (Meinicke, third modification) is more difficult to influence by antisyphilitic treatment than is the Wassermann. The latter was negative more frequently. The D.M. is of great importance in connection with the Wassermann especially where the latter is negative. The time of observation must be forty-eight hours. The results were better with D.M. and active serums than with inactive serums. There was no parallelism between the nonspecific results of active serums with the Wassermann test in those with D.M. The fresh serum showed no flocculation in several instances but the inactive did flake. It is recommended that inactive serum be used in conjunction with the active serum as the technic is only slightly increased in difficulty but the time for the test is shortened and the sensitiveness is greatly increased. Nonspecific results do not appear in these instances. The D.M. is very suitable for use in the diagnosis of syphilis, in spite of the fact that it is difficult to perform and the results are sometimes not specific. An exclusively colloid chemical aspect cannot be given the flocculation reaction for the diagnosis of syphilis. A certain colloid chemical reaction is necessary for the precipitation of the floccules. This is especially true in the D.M. and Sachs-Georgi reaction, and less so in the Wassermann test. The flakes will not appear if the colloidal mixture of the serum is not concentrated enough. They will remain in solution and the lipoid combination with the antilipoid will not be visible to the eye.

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**The Condition of the Albumin and Globulin in the Serologic Test for Demonstration of Syphilis.**

*Hans Sahlmann, Ztschr. f. Immunitätsf. u. exper. Ther., 33:130, Jena, Nov. 18, 1921.*

The precipitate of the characteristic flocculation test for syphilis is supposed to consist of lipoids, either in part or entirely. The lipoids are from the organ extracts. It appears that the globulin does not play an important rôle in the Wassermann or flocculation reactions so far as the substance in which the active principles are contained is concerned. Systematic experiments were undertaken to analyze the resulting serum products after treatment with HCl and carbonic acid. The serum components resulting from this procedure were examined with the Sachs-Georgi flocculation reaction and compared with the Wassermann reaction. The separation with HCl of the globulin showed a positive flocculation. This effect is basically different from the separation produced with carbonic acid. The hydrochloric acid globulin affects the flocculation as often and in the same quantitative way as hydrochloric acid albumin. The former is sometimes stronger, sometimes weaker. The carbonic acid globulin has a uniformly weaker effect than the albumin and may even have none at all.

Active substances are present in the albumin as well as in the globulin, in the splitting of syphilitic blood serum with diluted HCl or CO<sub>2</sub> during the flocculation test according to Sachs-Georgi. The resulting globulin fractions contain the inhibitory substances when the test is made with carbonic acid. These may also be a hindrance in the active serum in the Sachs-Georgio reaction. The carbonic acid globulin solutions lose their inhibiting effects in the Sachs-Georgi reaction by the previous inactivation. It was also shown that the globulins obtained with precipitation of carbonic acid in the positive as well as in the negative series were antagonistic in effect. This antagonistic effect is thermolabile and may be destroyed by heating at 55° for half an hour. This is to be considered as a protective effect of the colloid which is exercised by the most labile components of the euglobulin fraction. Globulin from animal serums inhibits flocculation. This was demonstrated in experiments with the active serum of man, guinea-pigs, rabbits and sheep.

The hydrochloric acid globulin has a comparatively slight inhibitory effect in comparison with carbonic acid globulin. It may be concluded that there is a stabilizing effect as a result of the use of HCl, and that the globulin obtained in the Sachs-Georgi test with employment of HCl will show a more regular reaction. The effect of larger quantities of globulin was not specific. It may be supposed that the Wassermann and Sachs-Georgi reactions are based on similar peculiarities of syphilitic serum.

The substances in the serum which inhibit the reaction of Sachs-Georgi with active serum are removed in the weak precipitations, especially those associated with the carbonic acid effect. There is no resulting lack of effective substances in the globulin as a result of this procedure. We can recognize the real carrier in the globulin fraction of the flocculation reaction if we include the pseudoglobulin as well as the easily precipitated euglobulin in the general term globulin. The most labile part of the globulin has an antagonistic effect in the flocculation and may lead to nonspecific results in the Wassermann reaction.

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(1e—193)

**A Clinically Useful Method of Estimating the Quantity of Blood.**

*W. Griesbach, Deutsch. med Wchnschr., 47:1289, Berlin, Oct. 27, 1921.*

In order to determine the quantity of blood in human beings, the author uses Congo-red, which has the following advantages: (1) non-poisonous, (2) soluble in water, (3) being of high molecular weight, it passes very slowly through the blood vessels; (4) being like the blood-corpuscles, electrically negative, it is, therefore, not absorbed by the blood; it does not discolor the lips, etc. The method depends on the fact that the intravenous injection of the dyestuff can be colorimetrically determined. The blood should be carefully centrifuged and the serum then estimated colorimetrically in an Autenrich colorimeter. A simple calculation gives the quantity of blood. Any trace of hemoglobin in the serum should be previously checked by spectroscopic examination, and the determination must be made prior to the introduction of any fatty substances. The serum, in fact, should be presented in an absolutely clear condition. The weight of blood in a normal man is, on the average, 6.7% of the total weight of the body.

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(1e—194)

**Toxicity of the Blood after Asphyxia.**

*R. Pellegrini, Gior. di clin. med., 2:606, Parma, Oct. 30, 1921.*

Whether the blood of animals subjected to asphyxia (without causing death) acquires thereby any toxic properties, is a question that has prompted much experimental work by various investigators. A survey of the literature shows so many and varied flagrant technical flaws and deductive errors as to practically invalidate all reports published. The toxic properties of homologous normal blood have not always been taken into account; the effects of mere physical volume, exclusive of chemical or biologic properties, seems to have been entirely overlooked. The various methods of introduction of the toxic blood of asphyxia (subcutaneous, intraperitoneal, intravenous) have been used indiscriminately, and no allowances made for variations in absorption and possible neutralization of the poison. There was no general agreement as to the manner of causation of the asphyxia. Experiments were made at different times with blood serum, defibrinated blood, serum obtained by removal of the clot, and whole blood alkalinized to prevent coagulation, without the least inquiry into the necessarily different reactions yielded by these so widely different fluids. Also, different species of animals were used without any accepted standard or method of comparison. The time element was apparently considered of no value; the temperature of the injected blood was not constant; the previous condition of the animal's blood, irrespective of asphyxia, as well as the now recognized specific antagonisms between the bloods of definite different species, are elements which seem not to have mattered to the older investigators. Additional research on this important subject is therefore clearly necessary, with due consideration of all factors involved.

(1e—195)

**Effect of Temperatures above One Hundred Degrees on the Oxidizing Action of the Blood on Coloring Agents.**

*A. Benoit, Compt. rend. Soc. de biol., 85:995, Paris, Nov. 26, 1921.*

Oxidizing action of the blood on benzidin, guaiac, etc., is not alone diastasic; this action is not lost by bringing blood to the boiling point, but is destroyed by incineration. In a mercury bath whose temperature was raised 1° every half hour, capillary tubes, containing each 5 mg. blood, were immersed for thirty minutes; each tube corresponded to some point of a range between 150° and 230° C. On removal from the bath, each tube was pulverized and its contents exposed to benzidin and phenolphthalein, in presence of hydrogen peroxid, at ordinary temperature. Up to 210°, oxidizing action was not modified; between 210° and 220°, intensity was progressively diminished. Friable carbon appeared. At 225°, ability to oxidize the most sensitive reagents ceased. Reactions of the blood to coloring agents may aid in the medicolegal examination of blood in products of incomplete combustion.

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(1e—196)

**An Apparatus for the Estimation of Catalase.**

*Wm. H. Welker, J. Lab. & Clin. Med., 7:173, Dec., 1921.*

A special apparatus was constructed for shaking mixtures of blood and hydrogen peroxid uniformly, and for allowing a series of accurate determinations of the liberated gas simultaneously. The machine consists essentially of a support of  $\frac{3}{8}$ -inch pipe from which a board is suspended by four brass rods. The eccentric on the shaft of the driving wheel is connected with this suspended board by a rod having a flexible joint at the board end. The bottles used are 500 c.c. salt-mouth bottles, ground for glass stoppers. These bottles are supported by copper cans fastened to the board, and are held rigidly in the cans by means of thermos bottle springs. As ordinary rubber stoppers proved unsatisfactory for closing the bottles, some double length stoppers were made to order. These can be seated so firmly in the bottle necks that no gas leakage occurs. For measuring the liberated gas each of the bottles is connected with the top of a gas measuring tube by a rigid walled rubber tube. To the bottom of the gas measuring tube is connected a leveling bulb. The 6 gas measuring tubes with their leveling bulbs are supported by a special stand. Aluminum caps for screw-cap vials are used as containers for the blood.

The mode of operation is as follows: 75 c.c. of diluted  $H_2O_2$  (equal volumes of  $H_2O_2$  and  $H_2O$ ) are measured into each of the bottles. The samples (0.5 c.c.) of blood are then accurately measured into the aluminum caps. These are floated on the surface of the hydrogen peroxid by a pair of tongs. The stoppers are then placed firmly into the bottle necks. The stop-cocks on the bottles are opened and the level of the liquid in the gas measuring tube adjusted so that the reading is 0. The stop-cocks on the bottles are closed and shaking is commenced. Readings are taken every five minutes at atmospheric pressure. The results, corrected for temperature, barometric pressure and aqueous tension, may be plotted as curves.

(1e—197)

**Catalysis of Blood in Diseases of the Blood.**

*H. Strauss and G. Rannfelt, Biochem. Ztschr., 122:137, Berlin, Sept. 26, 1921.*

Catalysis takes place in human blood and is obviously associated with the stroma of the red blood-corpuscles. By means of fractional extraction, dialysis and absorption, Wäntig obtained an albuminoid body free from purin bases. It contains a sugar and probably iron and phosphoric acids. In pernicious anemia catalysis is said to undergo alteration. Catalysis is measured by the catalysis exponent, viz., the amount of hydrogen peroxid in grams which can be replaced by 1 c.c. of a 1% blood solution in 30 c.c. of a 1% solution of  $H_2O_2$ . The catalysis index is the exponent referred to 1,000,000 red blood-corpuscles.

The method is as follows: 10 c.c. of a 1% sterile blood solution (0.5 c.c. blood in 50  $H_2O_2$ ) are added to 30 c.c. of a neutral 1%  $H_2O_2$  solution. After two hours, the lively evolution of gas is interrupted with dilute  $H_2SO_4$  and the liquid titrated with a solution of  $K MnO_4$ , standardized with oxalic acid (1 c.c. to 2 mg.  $H_2O_2$ ). The catalysis exponent is obtained by deducting from 150 c.c.  $K MnO_4$  the number of cubic centimeters used up, and referring the remaining number of cubic centimeters to 1 c.c. of the blood solution. This result was controlled by direct measurement of the volume of gas in an azotometer.

Determinations were carried out with normal blood in various diseases accompanied by secondary anemia, in marked diseases of the blood (chlorosis, leukemia), and in pernicious anemia. The results show that with normal blood-corpuscles, as well as in secondary anemia, the catalysis index of 4.8 remains constant within certain limits. In pernicious anemia, the index reaches 9 and frequently double its normal value. In pathologic increase of the red blood-corpuscles, the index was found to be remarkably low. An exact explanation of these conditions is not yet available.

(1e—198)

**The Glycolytic Power of the Blood Measured in Vitro.**

*P. Mauriac and L. Servantie, Compt. rend. Soc. de biol., 85:1067, Paris, Dec. 10, 1921.*

The glycolysis produced by a few drops of blood upon a titrated solution of glucose was tested for normal individuals and for blood derived from cases of tuberculosis, diabetes, nephritis, cirrhosis of the liver and lymphatic and myeloid leukemia. In normal man, there is but little variation of the glycolytic power, the index extending from 1.10 to 1.60. No apparent effects are produced upon it by pathological conditions, even diabetes.

(1e—199)

**Methods for Determination of Blood Sugar.**

*R. Offenbacher and A. Hahn, Deutsch. med. Wochenschr., 47:1419, Berlin, Nov. 24, 1921.*

Blood was taken from the vein and Bangs' blotting-plates impregnated with it, with serum (sharply centrifuged), and with plasma (obtained by the addition of hirudin); 50% glucose in 300 c.c. tea was given. One hour later the experiment was repeated, and the glycemic quotient figured out. In blood the ascent was more marked than in serum or  
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plasma. It is probable that the red blood-corpuscles take part in the glycemic processes, although irregularly. At present it is still difficult to determine. Osmotic processes are not involved but probably processes of adsorption take place through the membranes of erythrocytes. It is assumed that the glucose is chemically bound in the blood-corpuscles in such a manner that its osmotic pressure as glucose is suspended, but its power for reduction remains intact. The determination of sugar in whole blood is more simple and more exact than that in serum or plasma, because it does not overlook the sugar present in indeterminable amounts in the red blood-corpuscles.

(1e—200)

**The Effect of Light on the Glycolysis of the Blood.**

*Robert Fritzsche, Schweiz. med. Wchnschr., 51:1018, Basel, Nov. 3, 1921.*

By glycolysis is meant the phenomenon, already observed by Claude Bernard, of a diminution of the sugar content of the blood as soon as the blood has left the vessels. The process, since that time, has been the subject of numerous investigations. It concerns a process of fermentation, which according to newer studies, rests on the splitting of grape sugar into lactic acid. According to Schlosse, further products of glycolysis are acetic acid and formic acid, and from the latter, carbon dioxid and water. The ferment is derived as a proferment from the leukocytes and activated by a substance from the pancreas.

The author has studied the influence of light on blood glycolysis in the hope of thereby being able to make an experimental contribution to the therapeutic effects of the sun's rays. He came to the conclusion that an intensive exposure to the sun checked the course of glycolysis; with less illumination, little or no inhibition was observed. It is impossible to determine whether this effect is due to preventing the action of the glycolytic ferment or to checking its formation.

Bering showed through his studies on the effect of light on ferments that by means of small amounts of Finsen, quartz blue or sunlight, an accelerating effect on peroxydases can be obtained if these are present in sufficient concentration.

If the light dose is increased, this effect is reversed, and checking and finally complete inhibition of the fermentative process results.

If it is firmly established that sunlight in large doses causes a very definite restriction of glycolysis, a question to be considered is whether the promotion of glycolysis could not be secured by the energy of light employed in proper doses.

(1e—201)

**Relation between Blood Viscosity and Cholesterin in Serum and Whole Blood.**

*Rouzaud and Thiéry, Compt. rend. Soc. de biol., 85:964, Paris, Nov. 26, 1921.*

The proportion of cholesterin in serum and whole blood is not identical. Two hundred individuals of both sexes, healthy and unhealthy, on ordinary diet and fasting, were examined. Viscosity being 2.3, serum cholesterin was 0.75 gm., whole blood cholesterin 0.92 gm., per liter. Viscosity being 6.8, serum cholesterin was 3.68 gm., whole blood cholesterin 2.30 gm., per liter. The relations may be expressed by  
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R, or the quotient obtained by dividing 100 times the proportion of serum cholesterin by the proportion for whole blood. From normal viscosity, the normal value of R should lie between 110 and 115. With a viscosity between 5.3 and 6, R varies from 120 to 125; with a viscosity of 3.9, 3.2 and 2.8, the corresponding values of R are 100, 97 and 86. With excessive cholesterinemia, R may rise to 150, even with slight increase in viscosity, but the relation still corresponds to viscosity. This may explain certain facts. The hydremia of terminal uremia may induce a low proportion of serum cholesterin, as it sometimes diminishes serum urea, the result not necessarily being due to diminished antitoxic power of the organism. This hydremia may probably, in certain cases, mask the excessive cholesterinemia usually conceded to be present in chronic nephritis. While the proportion of serum cholesterin is increased in hyperviscosity, it progressively decreases if hydremia induces hypoviscosity. In excessive cholesterinemia occurring in lithiasis, a decrease in viscosity permits a corresponding decrease in the proportion of serum cholesterin.

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**Relation between Viscosity and Uric Acid in Serum and Whole Blood.**

*Rouzaud and Thiéry, Compt. rend. Soc. de biol., 85:962, Paris, Nov. 26, 1921.*

Uric acid is present in different amounts in plasma, serum and whole blood. Analyses, by Grigaut's method, in 120 individuals show that plasma contains 28 to 75 mg. per litre; serum, 37 to 99 mg., whole blood, 56 to 98 mg. The larger proportion in whole blood indicates an affinity for red cells and therefore a certain parallelism between uric acid and viscosity. Viscosity determines the proportion of uric acid in the serum and whole blood, and not the absolute quantity. In hyperviscosity, the serum contains little as compared with the whole-blood content; in hypoviscosity (anemia or hydremia) the proportion in the serum equals, or rarely, exceeds that of the whole blood. In normal individuals presenting no uricemia, variations in viscosity produce differences of only a few milligrammes in the uric acid of the serum. In marked uricemia, hypoviscosity may considerably increase the uric acid of the serum. Untoward effects produced by hydremia may possibly be due to this fact. The relation R may be expressed as the quotient obtained by dividing 100 times the proportion of serum uric acid by the proportion for the whole blood. For normal viscosity, the value of R lies between 60 and 66%; it may fall to a value of 35 to 38% when viscosity exceeds 6; it may rise to a value of 80 to 85% when viscosity is 3.6 or 3.2. In one case, viscosity falling to 2.8, the value of R was 109%.

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**Clarification of Blood by Tungstic, Metaphosphoric or Trichloracetic Acid.**

*C. Guillaumin, Compt. rend. Soc. de biol., 85:1043, Paris, Dec. 10, 1921.*

If sodium tungstate plus sulphuric acid be used to remove albumin from the blood, a considerable excess of tungstic acid should remain in the solution after albumin has been coagulated. The filtrate should possess a minimum acidity below which there is little or no coagulation

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in the cold. An effort has been made to determine the exact acidity proper for complete removal of albumin, which corresponds to 4.8 phenolphthalein. The degree of acidity can be verified colorimetrically by superposing 40% alkaline methyl red on 60% acid methyl red. The proportions necessary are: serum or plasma, 1 vol.; 10% solution sodium tungstate, 1 vol.; distilled water, 7 vol.; two-thirds normal sulphuric acid, 1 vol. For corpuscles the proportions are: corpuscles, 1 vol.; sodium tungstate, 2 vol.; water, 5 vol.; two-thirds normal sulphuric acid, 2 vol. The solutions should be agitated and filtered. For ordinary whole blood, the proportions given for serum are satisfactory, but the acidity is not sufficient for blood very rich in corpuscles. In this case, decinormal sulphuric acid should be added, drop by drop, until the phenolphthalein value of 4.8 has been reached or slightly exceeded. As anticoagulants, pure sodium fluorid and potassium oxalate have no effect, sodium citrate increases the alkalinity. Sodium metaphosphate plus HCl will give satisfactory results if used as follows: plasma, 5 c.c.; 5% solution sodium metaphosphate, 1.2 c.c.; water, about 40 c.c.; HCl, 13.25:1,000, (36 c.c. pure HCl per liter), 1.2 c.c.; water, to make 50 c.c. For corpuscles the quantities are: corpuscles, 5 c.c. (or 10 c.c. of their 50% dilution); 5% metaphosphate, 2.2 c.c.; water, about 30 c.c.; HCl, 13.25 parts per 1,000, 2.2 c.c.; water, to make 50 c.c.; agitate and filter. In clearing by the use of an equal volume of trichloracetic acid dilution, the proportion of acid is usually 20% and must not be below 8% to remove albumin completely in the cold. In estimating nitrogenous substances which are not of the urea group, higher figures are given by the tungstic and metaphosphoric filtrates; the results are lowered by greater acidity. The trichloracetic acid filtrate gives lower results, but with less variation because of differences in acidity. The problem is complex because there are 2 factors, namely, variation in acidity due to adsorption, and the nature of the clearing agent, which produces compounds more or less soluble. Trichloracetic acid is better for clinical use; the other two methods are more exact.

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(1e—204)

**The Micro Determination of Calcium in Whole Blood, Plasma and Serum by Direct Precipitation.**

*Guy W. Clark, J. Biol. Chem., 49:487, Dec., 1921.*

Clark's method is as follows: Whole Blood. With a pipet, place 5 c.c. of citrated whole blood in a 25 c.c. volumetric flask; with the same pipet, add two 5 c.c. portions of warm water (about 65° C.); mix and allow to stand twenty minutes or longer. Add 5 c.c. of 1% ammonium chlorid; make up to volume with distilled water, mix thoroughly, and transfer to a 50 c.c. centrifuge tube. Cover the tube with rubber dam or paraffined paper and centrifuge at high speed for twenty minutes. With a pipet, remove 15 c.c. or if possible 20 c.c.; transfer to a 50 c.c. centrifuge tube and, while rotating the tube to agitate the liquid slowly, add 4 c.c. of 3% ammonium oxalate; mix thoroughly, and allow to stand over night. Centrifuge for five minutes at 1,800 r.p.m. Completely remove the supernatant liquid by means of a siphon, stir up the precipitate with a fine stream of cold, distilled water, wash down the walls of the tube, using in all approximately 35 c.c. of water. Centrifuge immediately and completely siphon off the wash water. Dissolve the precipi-

tate in 5 c.c. of approximately normal sulphuric acid, heat to 75° C., and titrate with 0.01 normal potassium permanganate.

Plasma or Serum. Place 1-5 c.c. of citrated plasma (or serum) in a 50 c.c. centrifuge tube and, while rotating the tube, slowly add 3% ammonium oxalate, equal in volume to one-half the amount of serum or plasma. Mix thoroughly and allow to stand over night. The remainder of the procedure is the same as that described for whole blood. Reagents are prepared as follows: Potassium permanganate, approximately 0.01 N: After dissolving the salt in the proper amount of water, the solution should be heated on a steam bath for thirty-six to forty-eight hours, or allowed to stand at room temperature for ten days or more. The solution is then filtered through asbestos and stored in amber bottles. The standardization is best made with sodium or calcium oxalate. The oxalates are dissolved in and made up to volume with approximately N sulphuric acid. Small portions (5-10 c.c.) are then measured into 50 c.c. centrifuge tubes, heated to 75° C. and titrated.

Ammonium chlorid (1% solution): This reagent should be tested for calcium as follows: 10 gm. are placed in a platinum dish and sufficient heat is applied to volatilize the ammonium chlorid. The ash is dissolved in a minimum amount of hot 6 N hydrochloric acid (previously tested for calcium) and the calcium precipitated by a modification of McCrudden's method. Sulphuric acid, Approximately normal: Add 28 c.c. of concentrated c.p. sulphuric acid to 970 c.c. of distilled water. Sodium acetate, (20% solutions): If several lots of this reagent are available, qualitative tests should be made and the sample selected which shows the smallest amount of calcium. Dissolve the salt (200 gm. of the crystalline salt in a final volume of 1,000 c.c.) in nearly the required amount of distilled water; add 0.5% ammonium oxalate (this salt should be dissolved in a minimum amount of water) and bring to volume. Place in a refrigerator (10°-12° C.) and allow to stand for forty-eight hours, stirring daily. Centrifuge and store in paraffin-coated bottles. Dilute hydrochloric acid: Test the concentrated acid by evaporating 25 c.c. in a platinum dish. Evaporate almost to dryness (leave 1 small drop); dilute to 5 c.c. and precipitate the calcium in the regular way. Ammonium hydroxid, approximately 2 N., is best prepared by passing pure ammonia gas into conductivity water. The strength is determined by titration and the desired normality, obtained by dilution.

The author's experimental data shows that his method is accurate to  $\pm 5$  per cent.

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(1e—205)

**A Note on the Estimation of Blood Chlorids in Tungstic Acid Filtrates.**

*John B. Rieger, J. Lab. & Clin. Med., 7:166, Dec., 1921.*

In the titration (by the Volhard method) of chlorid from the tungstic acid filtrate obtained in the Folin-Wu system of blood analysis there need not, as Whitehorn, supposes, be any loss of silver. The purin derivatives are never precipitated under these conditions, and silver begins to settle out only when the concentration of sodium tungstate in the filtrate reaches 50 mg. per 100 c.c. Filter paper that contains chlorid must not be used. Check analyses on mixtures of pure

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sodium chlorid and sodium tungstate, the latter in concentrations of 25 mg. per 100 c.c., have always given results within 1% of the theoretic value, whether the silver chlorid was removed by filtration or centrifugalization.

In precipitating the proteins of whole blood, the addition of acid before dilution with water is recommended. This does not change the distribution of chlorid, if the blood be allowed to stand for an hour. This is especially advantageous when a nonprotein nitrogen determination is to be made, because, if filtered immediately, the liquid will sometimes foam and destroy the result. Oxalate is preferred to citrate for preventing coagulation, because the latter interferes with the alkalimetry of the blood.

The filtrate will always contain tungstic acid, but this is an advantage because it inhibits the coagulation of the precipitated chlorid, until the mixture has been diluted to the mark and shaken vigorously. Any silver chlorid occluded under these conditions will not influence the results of titration, since this is made on aliquots.

(1e—206)

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**Relation between the Chlorid Content of the Blood and Its Volume Per Cent of Cells.**

*A. Norgaard and H. C. Gram, J. Biol. Chem., 49:263, Dec., 1921.*

The experiments here reported were undertaken to determine the relation between the chlorid content of the blood and its cell volume percentage. The examination of the blood was based on a micro determination of the chlorids and a determination of the volume of the blood cells. The chlorid content of the blood was calculated as sodium chlorid and the results tabulated in per cent. of 100 gravimetric parts of the whole blood or plasma. In 52 cases of various types, the authors found that the content of sodium chlorid in the plasma was nearly constant, (about 0.61%), but the corresponding chlorid determinations on whole blood showed that these values varied greatly. The authors observed that the chlorid percentage in blood increases when the cell volume percentage (and hemoglobin) drops, and vice versa. The explanation of this phenomenon must be sought in the fact that the blood corpuscles contain a smaller percentage of chlorids than the plasma. The chlorid content of the blood corpuscles the authors found to be nearly constant, (about 0.31%), the only serious divergence being found in pernicious anemia, where the average content is calculated to be 0.23%.

(1e—207)

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**Sulphates in Blood.**

*W. Denis, J. Biol. Chem., 49:311, Dec., 1921.*

To determine inorganic sulphates in normal human blood the procedure is as follows: 5 c.c. oxalated blood or plasma are treated with 5 c.c. 0.1 N hydrochloric acid, 5 c.c. 5% mercuric chlorid solution, and 0.3 gm. finely powdered mercuric chlorid. The mixture is then shaken vigorously for five minutes, and at intervals for one hour, and is then poured on a small dry ashless filter. Then 5 c.c. of this filtrate, which should be absolutely clear, are treated with 1 c.c. of a 1% solution of ammonium nitrate and 1 c.c. of the acidified barium chlorid solution described below, and the turbidity so produced is (Sec. 1—Page 372)

compared after an interval of ten minutes with a standard prepared by adding to 10 c.c. of a standard solution of potassium sulphate 10 c.c. of 5% mercuric chlorid solution, 4 c.c. of 1% ammonium nitrate, and 4 c.c. of 1% barium chlorid solution. This technic gives excellent results with normal material, but with pathologic specimens the amount of sulphate present is sometimes so much increased that it is impossible to obtain a colloidal suspension of barium sulphate which will not precipitate. In such cases it is desirable, if a sufficient amount of material is available, to employ the technic described for use with animal blood. This is as follows: The blood is collected by venous puncture and coagulation prevented by means of powdered sodium citrate (30 mg. per 10 c.c. of blood). To 10 c.c. of blood or plasma contained in a 200 c.c. Erlenmeyer flask are added an equal volume of 0.02 N hydrochloric acid and after an interval of five minutes 30 c.c. of 5% mercuric chlorid containing 5 c.c. concentrated hydrochloric acid (sp. gr. 1.178) per liter. After vigorous shaking, the mixture is allowed to stand for one hour and is then filtered through a dry 11 c.c. filter paper. For this filtration the use of a high grade of ashless filter paper is essential. For the determination of total inorganic sulphates 10 c.c. of the clear filtrate (equivalent to 2 c.c. of whole blood or plasma) are pipetted into a 100 c.c. beaker, and to this are added 5 c.c. 1% ammonium nitrate, and with stirring 5 c.c. 1% barium chlorid containing 5 c.c. concentrated hydrochloric acid per liter. (This is the acidified barium chlorid solution referred to above.) After a period of ten minutes the colloidal suspension of barium chlorid is compared to a standard which has been prepared simultaneously with the unknown in the following manner: To 10 c.c. of a standard solution of potassium sulphate (equivalent to 0.10 mg. sulphur) are added 10 c.c. of the acid mercuric chlorid solution, 10 c.c. 1% ammonium nitrate, and 10 c.c. 5% barium chlorid. To calculate the results, the reading of the standard (usually 20) is divided by the reading of the unknown and the dividend multiplied by 50. This will give the result expressed as milligrams of sulphur per 100 c.c. blood.

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**The Fate of Sulphids in the Blood.**

*Howard W. Haggard, J. Biol. Chem., 49:519, Dec., 1921.*

The object of this investigation was to determine in what manner hydrogen sulphid is transported in the blood after inhalation of this gas. That it is transported in the blood in a loosely combined and readily dissociable manner is evident from the fact that when hydrogen sulphid is injected into any of the body cavities, it is almost at once detectable in the expired air. The author performed experiments to study (1) the action of hydrogen sulphid upon sodium bicarbonate solution; (2) the action of hydrogen sulphid upon plasma; (3) the reaction between hydrogen sulphid and plasma or blood; (4) the reaction of sodium sulphid with blood and plasma; (5) the detoxication of sodium sulphid by plasma; (6) the effect of repeated intravenous injection of sodium sulphid. Dogs were used in all the experiments except (1). It was found that when an atmosphere containing hydrogen sulphid is inhaled no combination of the gas is formed with the hemoglobin of the blood nor is any appreciable amount of sodium sulphid formed in the plasma. The phenomena of the disease of sulph-

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hemoglobinemia have no significance for the normal transport of sulphid. Blood plasma in the presence of oxygen possesses the property of rapidly oxidizing hydrogen sulphid. The products of oxidation combine in part with the sodium of the plasma. Sodium sulphid is rapidly and completely hydrolyzed by blood or plasma. The absence of oxygen was found to have no effect upon this process. If oxygen be present, however, a large part of the liberated hydrogen sulphid is oxidized. The reduction of blood by hydrogen sulphid or sodium sulphid is the result of the withdrawal of oxygen from the corpuscles for the oxidation of the hydrogen sulphid. The rate of oxidation of hydrogen sulphid in the blood is such that in a comparatively short period many times the lethal amount of sodium sulphid may be administered intravenously to animals without any apparent effect.

(1e—209)

**The Composition of Cytozym and Action of Phosphatids in the Coagulation of the Blood.**

*E. Zunz and J. la Barre, Compt. rend. Soc. de biol., 85:1107, Paris, Dec. 10, 1921.*

The cytozyme of Bordet and Delange contains phosphatids of the lecithin and cephalin types, and sometimes amino-acids or peptids. This preparation is replaceable by Levene's cephalin. Rapid coagulation is produced by mixing, in the presence of calcium, a small quantity of cephalin with serum, and adding, after a few minutes, either dilute oxalated plasma or a solution of fibrinogen. The clot-producing property of Levene's lecithin may be greatly enhanced by adding a small quantity of cephalin. Levene's cephalin may be separated, by absolute alcohol and centrifugation, into 2 portions, of which the part insoluble in alcohol, toluol, etc. represents true cephalin. The soluble portion resembles Bordet and Delange's cytozym. For this preparation the authors suggest the name of "cytozymin". Cytozymin, added to serum in the presence of calcium, causes the latter to coagulate if mixed with dilute oxalated plasma or fibrinogen. True cephalin will not produce this result, but aids the action of cytozymin, like lecithin, glycocoll and triglycerin.

(1e—210)

**The Estimation of Inorganic Phosphorus in Blood Plasma by the Method of Bell and Doisy.**

*Burton A. Myers and Marian C. Shevky, J. Lab. & Clin. Med., 7:176, Dec., 1921.*

The authors found, in using the Bell-Doisy method, that the depth of blue color which appears is not directly proportional to the amount of phosphorus actually present. Bell and Doisy state that it may be necessary to use a stronger standard or less filtrate in bloods that contain much phosphorus, but they give no data as to the permissible difference between the standard and the unknown, an important point in the actual use of the method. Phosphorus in the serum of normal persons may, according to Greenwald, vary between 1 and 7 mg. in 100 c.c. and may be much greater in pathologic conditions.

The authors made a series of solutions of acid potassium phosphate ( $\text{KH}_2\text{PO}_4$ ) within the range of concentration in which inorganic phosphorus is known to exist in protein-free plasma filtrates. The solu-

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tion containing 0.5 mg. of phosphorus in 100 c.c., probably about the average phosphorus concentration of plasma filtrates, was taken as a standard. The following table gives the estimated amounts.

Actual P concentration	P Concentration found	Error
Mg. per 100 c.c.	Mg. per 100 c.c.	%
2.00	1.73	-13.5
1.75	1.56	-10.9
1.50	1.35	-10.0
1.25	1.08	-14.0
1.00	0.85	-15.2
0.75	0.67	-10.7
0.25	0.25	± 0.0

The figures show that the only solution in which a correct determination was made was the one weaker than the standard, and that all the other readings were too low by considerable amounts. Further investigation with known phosphate solutions showed that the phosphorus could be estimated with fair accuracy when the concentration of the standard was not more than 0.25 mg. of phosphorus per 100 c.c. greater than the unknown. Consequently, in working with unknown solutions it is necessary to have a series of standard solutions, and to select a standard with a concentration of not more than 0.25 mg. per 100 c.c. greater than the concentration of the solution to be determined. It was also found that many rabbit plasmas and some human plasmas gave little or no color unless more than the usual amounts of molybdic acid and hydroquinon were added; but the reaction appeared when 1.5 c.c. of molybdic acid and 3 c.c. of hydroquinon were added to 5 c.c. of plasma filtrate diluted 1:5. This modification had no effect on the color produced, hence, inasmuch as some human plasmas have this peculiarity, the modification should be adopted.

A small series of determinations of inorganic phosphorus in filtrates from plasma and beef serum, before and after known amounts of phosphorus were added, showed that the method, as modified by the authors gave errors ranging from 2.3 to 10%. The average error was ±6%.

(1e—211)

**The Protein Content of the Whole Blood and Plasma in Cancer.**

*Ruth C. Theis, J. Cancer Res., 6:127, April, 1921.*

Theis examined 43 blood specimens, the nitrogen of the whole blood, serum, or plasma being determined by the Kjeldahl method, and the hemoglobin with Dare's hemoglobinometer. She concludes that the proteins of the blood plasma are neither decreased nor increased in those suffering from cancer as compared with other hospital patients.

(1e—212)

**Blood Fibrin Studies. I. An Accurate Method for the Quantitative Analysis of Blood Fibrin in Small Amounts of Blood.**

*D. P. Foster and G. H. Whipple, Am. J. Physiol., 58:365, Jan. 1, 1922.*

The authors estimate the fibrin in whole blood by determining the red cell hematocrit. The technic of the method is as follows: Approximately 9 c.c. of blood are collected by needle from the vein into a vase-  
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lined syringe and delivered immediately into a 15 c.c. hematocrit tube which contains 1 c.c. of 1% sodium oxalate solution. The tube with its contents is immediately inverted twice to insure thorough mixing. The mixture is centrifuged at high speed (3,000 r.p.m.) for thirty minutes. The amount of cellular elements and plasma are read to tenths of a cubic centimeter. Exactly 2 c.c. of the plasma are delivered by a calibrated pipet into a tumbler containing 40 c.c. of an 0.8% solution of sodium chlorid, and 2 c.c. of a 2.5% solution of calcium chlorid. A similar duplicate sample is set up. The preparations are thoroughly mixed and allowed to stand at room temperature for two hours. To some abnormal blood plasmas, it is necessary to add normal serum and a longer period may be required to insure complete coagulation. The fibrin is freed from the fluid elements by gentle manipulation and pressure with a glass rod. The fibrin mass thus obtained is then washed in distilled water. The clear free fibrin is then placed in a small porcelain crucible and dried in an oven at 110° C. to a constant weight. This requires from three to ten hours, depending on the amount of fibrin. After drying, the crucible is placed in a desiccator and allowed to cool. The weight of the crucible is recorded to tenths of a milligram. The fibrin is then ignited in the crucible over a Bunsen flame (fifteen minutes combustion time). While still warm, the crucible is placed in a desiccator. When cool, it is reweighed. The difference in the weights before and after burning is the weight of fibrin for the sample analyzed. Knowing the weight of fibrin per cubic centimeter of plasma and the ratio of red blood cells to plasma, one may calculate the amount of fibrin in 100 c.c. of whole blood or blood plasma.

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**Blood Fibrin Studies. II. Normal Fibrin Values and the Influence of Diet.**

*D. P. Foster and G. H. Whipple, Am. J. Physiol., 58:379, Jan. 1, 1922.*

By means of the authors' method, described in the preceding paper, it is possible to make accurate fibrin determinations in duplicate using but 8 to 10 c.c. of whole blood. One may therefore make frequent fibrin determinations in animals without any complications due to anemia. In the recorded observations dogs were used. They were fed once daily and blood samples taken before the food or diet mixture was given. The authors' tabulated results show that fibrin is a blood plasma protein which is very labile. The average figures for dogs on a mixed diet were found by Foster and Whipple to be about 400 mg. fibrin per 100 c.c. plasma. Individual dogs under uniform conditions have a relatively constant fibrin level. Fluctuations should not exceed 20 to 25%. Fasting conditions give more stability to the blood fibrin values and the physiological fluctuations are less. A level is usually reached in dogs after a three-day fast. The authors remark that normal blood plasma fibrin values should fall within the limits of 250 to 500 mg. per 100 c.c. plasma. The figures for whole blood should always be given, as this is the efficient fibrin level which concerns hemorrhage. In normal dogs this figure is a little less than one-half the plasma values as the red cell hematocrit is usually 50 to 57%. The authors found that diets rich in animal protein (meat, liver, etc.) favor a high blood fibrin level as contrasted with fasting, fat or carbohydrate feeding.

A diet of cooked pig stomach caused a rise in the blood fibrin level of about 100% over the dog's fasting level. It was also observed that thyroid feeding sufficient to cause loss of weight may be associated with a slowly decreasing level of blood fibrin.

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**Blood Fibrin Studies. III. Fibrin Values Influenced by Transfusion, Hemorrhage, Plasma Depletion and Blood Pressure Changes.**

*D. P. Foster and G. H. Whipple, Am. J. Physiol., 58:393, Jan. 1, 1922.*

The greater number of these experiments were done with the primary object of investigating changes in the volume of the circulating blood. As a part of this work, blood samples were taken both for fibrin estimation and for blood volume determinations at various intervals. Solutions of inert red dyes were likewise introduced as a part of the blood volume estimation. The influence of these procedures upon the fibrin values is shown by the authors in a control experiment in which the usual dye injections and blood sample removals were performed at the usual time intervals without any injection, transfusion or hemorrhage. The tabulated results of this control experiment show a fibrin level which remains practically unchanged throughout the period of observation. In the other experiments the particular solution employed was injected by hypodermic needle inserted into the jugular vein. The authors found that plasma fibrin values may be modified by large intravenous injections of Locke's solution. Subsequently there is a rise above the normal level, best explained by the stimulating action of the salts. Injections of acacia were found to produce similar dilution of the fibrin values depending upon the amounts of solutions introduced. A slow rise of the fibrin values to normal follows. A reaction similar to that observed in the acacia experiments followed the intravenous injection of normal serum. In one of the authors' experiments plethora was induced by means of whole blood transfusion. An unexplainable fall in fibrin values was noted 1 1/2 hours after the injection of whole blood. Fibrin may be washed out of the circulation by simultaneous bleeding and intravenous injection of a red cell serum mixture, but there is a return to normal fibrin values in twenty-four hours. Hemorrhage with or without saline transfusion will cause wide fluctuation in fibrin values. Blood pressure changes do not, by themselves, modify the amount of circulating fibrinogen in the plasma.

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**Blood Fibrin Studies. IV. Fibrin Values Influenced by Cell Injury, Inflammation, Intoxication, Liver Injury and the Eck Fistula. Notes Concerning the Origin of Fibrinogen in the Body.**

*D. P. Foster and G. H. Whipple, Am. J. Physiol., 58:407, Jan. 1, 1922.*

In the studies embraced by this paper, dogs were used as the experimental material. The authors determined the influence on the blood fibrinogen of the following: (1) sterile abscess, produced by the subcutaneous injection of 1 c.c. sp. turpentine; (2) administration of toxic proteoses; (3) Roentgen ray injury; (4) acute infection; (5) (Sec. 1—Page 377)

chloroform injury of the liver; (6) phosphorous and hydrazin injury of the liver; (7) sterile abscess plus chloroform injury; (8) Eck fistula operation. The authors' tabulated results show that tissue injury and inflammation stimulate fibrinogen production and cause a marked injury increase in fibrin values, whether the inflammation be septic or sterile. Concerning the effect of toxic proteose administration, Foster and Whipple found that such a procedure increases the fibrin values if sub-lethal doses are administered. Exposure to Roentgen rays, whether over the abdomen (lethal) or over the thorax (non-lethal) was found by the authors to give a prompt rise in blood fibrin. Following the thorax exposure the authors could demonstrate a definite cell injury in the lymphatic tissues and bone marrow of ribs and vertebrae. The highest values in blood fibrin were found in the animals suffering from acute infections. The administration, in small doses, of chloroform, phosphorus and hydrazin caused a rise in fibrin values, but larger doses of these liver poisons are depressing and if sufficient liver parenchyma is injured a fall in fibrin values results. The combination of liver injury (depression) with an abscess reaction (stimulus) was found to result as follows: If the liver injury was severe an initial fall in fibrin values occurred. After the second day of injury, the regenerating liver could be stimulated to great production of fibrinogen by appropriate stimuli (abscess). Without this stimulus the liver maintains but a low fibrin level during its period of repair. The authors found that in general the Eck fistula liver reacted like the normal liver in its fibrinogen production.

In discussing the origin of fibrinogen in the body, the authors dismiss, as possible sources, the intestinal tract and bone marrow. They point to the uniform low fibrin values following acute extensive liver injury and the parallelism between the extent of the liver injury and the depression in fibrin values. They have shown experimentally that the repairing or regenerating liver is usually associated with low fibrin values, but an over-production of fibrinogen will follow an appropriate stimulus (abscess) to the liver. The authors believe that this and other evidence points to the liver as the only actively productive source of fibrinogen, although the possible presence of limited reserve supplies in other body tissues is admitted.

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**A New Method for the Determination of the Fibrin Percentage in Blood and Plasma.**

*H. C. Gram, J. Biol. Chem., 49:279, Dec., 1921.*

Gram says a practical method for determining the fibrin (fibrinogen) percentage must fulfill the following conditions: (1) Quantities of blood must be used which may be easily obtained several times without inconvenience to the patients. (2) A determination of the percentage both in plasma and in blood must be allowed. (3) The complete precipitation of the fibrin (fibrinogen) must be controlled. (4) Fibrinolysis must be excluded. (5) The fibrin and fibrinogen must be pure, and cellular elements, which may either increase the weight or cause fibrinolysis, should not be included. The technic for determining the fibrin content is as follows: About 4.5 c.c. venous blood are run into a graduated 5 c.c. centrifuge tube divided into tenths of a cubic centimeter and containing 0.5 c.c. 3% sodium citrate. The citrated (Sec. 1—Page 378)

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blood is shaken and the blood adhering to the cork and upper part of the glass is wiped off. After the specimen has stood for some time, the corpuscles have sedimented sufficiently to draw off 0.025 c.c. of plasma for the platelet count and 0.4 c.c. for the determination of the coagulation time. The velocity of this sedimentation depends upon the cell volume percentage and the fibrinogen percentage in the plasma. The specimen is then centrifuged for ninety minutes at 3,000 revolutions per minute, and the amount of citrated blood and precipitate then noted, the cell volume being calculated by the equation: Volume percentage =  $P \times 100 \div B$ , "P" being the precipitate in c.c. "B" being blood in c.c. The clear cell-free citrated plasma is drawn off with a pipet, and 2 c.c. are transferred into a 50 mm. wide cylindrical vessel, the bottom of which is slightly rounded off against the sides. Then 9 c.c. 0.9% sodium chlorid and 2 c.c. 1%  $\text{CaCl}_2 \cdot 6 \text{H}_2\text{O}$  solution are added and the vessel is placed in the thermostat at  $35^\circ \text{C}$ . for one and a half hours. When the glass is taken out the contents will always be found clotted, except possibly in very severe cases of hemophilia or melena neonatorum. After the clot is loosened it is thrown out on several layers of filter paper on which it forms a jelly-like cake. The water is absorbed very quickly by the paper, leaving a round shining membrane, which may easily be attached with a glass rod when the top layer of paper is thrown into a jar of water. The detached membrane is kept in distilled water for fifteen minutes and is then transferred into absolute alcohol for five minutes and finally into ether for another five minutes to dehydrate and extract lipoids. The hardened, dehydrated fibrin, which resembles a piece of paper is gripped by wire pincers of known weight and hung in the thermostat for some hours or in an oven for a shorter period. When the weight is constant, the fibrin is weighed either on the analytic balance or on a fine torsion balance. In the cylindrical glass vessel there is always left a small amount of liquid (diluted serum), which may be used as a control, since clotting either spontaneously or by addition of a little serum, shows that the precipitation of the fibrinogen has not been complete. Gram found this control test so delicate that positive results were given with less than 0.25 mg. fibrin. In order to calculate the fibrin percentage in plasma (F<sub>p</sub>) and blood (F<sub>b</sub>) a knowledge of the following values is necessary: Wf<sub>2</sub>=Weight in grams of fibrin in 2 c.c. citrated plasma. C<sub>b</sub>=Citrated blood (0.5 c.c.). C=Citrate (0.5 c.c.). P=Cell precipitate, in cubic centimeters. The formula for calculating the percentage in pure plasma is:  $F_p = [(C_b - P) \times Wf_2 \times 100] \div (C_b - C - P) \times 2$ . The corresponding formula for the percentage in pure blood is:  $F_b = [(C_b - P) \times Wf_2 \times 100] \div (C_b - C) \times 2$ .

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**Absence of Prothrombin in Aqueous Organic Extracts.**

*P. Nolf, Compt. rend. Soc. de biol., 85:1116, Paris, Dec. 10, 1921.*

For studying coagulation effects of organic, aqueous extracts, simple maceration in distilled water or normal saline is not sufficient. The cellular substances are not readily diffusible. The pulp of the organ must be washed free of blood and finely ground, mingled with sand or glass wool, in a small quantity of isotonic NaCl solution. Insoluble matter may be removed by the centrifuge. Extracts obtained in this manner slowly, but invariably, coagulate solutions of fibrinogen in the presence of calcium. However, it should be remembered that the organ,

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though free of blood, still contains lymph, whose proteins are the same as those of blood serum. Proteins of organs thus prepared are both cellular and humoral, and distinction between their effects is difficult. The author has endeavored to obtain complete removal of the lymph, as well as of the blood, by working with hearts of fish, birds and mammals. Irrigation was continued for a long time and extracts prepared from hearts so irrigated, and which had been allowed to continue beating for three to four hours, no longer coagulated fibrinogen in the presence of calcium. The experiments show that parenchymatous cells do not contain prothrombin as a cell constituent.

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Determination of the Acetone Bodies in Blood.

Roger S. Hubbard, *J. Biol. Chem.*, 49:375, Dec., 1921.

This method of Hubbard is based on experiments with lead and sodium hydroxid described by him in the preceding paper (*J. Biol. Chem.* 49:357, 1921). An amount of blood which varied from 1 to 5 c.c. was measured into a 100 c.c. shaking cylinder, and water was added to give a volume of between 40 and 50 c.c. Then 50 c.c. of colloidal iron were added, and the solution was thoroughly shaken. Next, 10 c.c. of Goulard's extract were added, and the solution was shaken again. Finally, enough sodium hydroxid was added to precipitate the lead, the solution again thoroughly mixed, and allowed to stand for about one hour. It was then diluted to the mark and centrifuged in tubes covered with rubber caps to prevent loss of acetone. The supernatant liquid was then poured through filter paper, and an aliquot used for the analysis. The filtrate was clear, gave no precipitate of lead with sulphuric acid, or of protein with sulphonesalicylic acid, and contained very little reducing substances when tested with alkaline picrate solutions even when the concentration of blood sugar was as high as 0.3%. Hubbard says the amount of sodium hydroxid that should be used must be determined by preliminary experiment for each batch of Goulard's reagent as the lead content of this reagent varies somewhat. The proper amount to use is the smallest amount of sodium hydroxid which will precipitate the lead from solution. The filtrate from the precipitation of lead with sodium hydroxid should react alkaline to litmus, but only faintly alkaline to phenolphthalein. An aliquot of the filtrate was used for the determination of the acetone bodies. If only 5 c.c. of blood were available for the determination, the aliquot taken was usually 50 c.c. When more blood was available, 2 or 3 separate precipitations were carried out as described, and the filtrates combined. In all cases the solution was diluted, for the determination, to a final volume of 150 c.c. The analysis was carried out in the same way as that described by Hubbard for urine, except that it was found that a distillation of the distillate first obtained from an excess of sodium hydroxid before treatment with sulphuric acid plus potassium permanganate gave more consistent results. Subsequent distillations from sulphuric acid plus potassium permanganate and from sodium peroxid were carried out as described in the preceding paper. For the final determination, the author believes it is advisable, in most cases, to use 10 c.c. of an iodin solution, 1 c.c. of which is equivalent to 0.02 mg. of acetone, and titrate with a solution of sodium thiosulphate which is one-half concentrated. In this case the correction to be added to the deter-

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mination of acetone from B-hydroxybutyric acid is 17 instead of 15%.

The author states the method gives a high and constant percentage of recovery for added acetone bodies, and gives good agreement between duplicate determinations. The results obtained by this method on blood from normal subjects are low, Hubbard says. The accuracy of the determination is about 0.1 mg. per 100 c.c. of blood.

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**The Relationship of Blood Groups to Disease.**

*J. Arthur Buchanan and Edith T. Higley, Brit. J. Exper. Path., 2:247, London, Dec., 1921.*

The writers draw attention to the fact that the possibility of a fixed relationship of "blood groups" to a particular disease or diseases has received practically no consideration. They briefly refer to the observations of workers since Eulenburg (1866) in regard to the agglutination property of erythrocytes. The data presented in the study is a review of the blood groups found in patients in the Mayo Clinic from January 1, 1917, to May 1, 1921. The relationship between blood grouping and disease can be seen in the first 17 tables. The figures have been carried out into percentages only when a considerable number of cases were available. A careful study of these tables shows that no relationship between blood group and malignancy exists, as suggested by Alexander. Also, there is no relationship between blood groups and any disease in which sufficient data are available to justify a conclusion. The percentages originally presented by Moss are approximate and capable of considerable variation, without special significance. When presenting statistical studies of blood-grouping, nationality should be considered.

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**Blood-Cells of the Crawfish (*Astacus Fluviatilis*).**

*L. Betances, Arch. d'anat. micr., 18:1, Paris, Oct. 15, 1921.*

Cytologic examination of dried blood is very difficult. Blood was obtained by section of a claw or antenna, or by an opening into the cardiac region of the carapace. For study of the unstained blood, a drop was placed between slide and cover-glass, either with no dilution or diluted with a drop of Ringer's solution, 5 to 9 per 1,000 NaCl or magnesium sulphate, 10 per 1,000 sodium citrate, tincture of iodin in water, or pure water only. For making dried preparations, a small drop is quickly spread to a thin layer and immersed in a 9:1,000 NaCl solution. After one or two minutes, the smear is gently washed in running water and fixed. This process must be rigidly adhered to. For staining, Pappenheim's May-Grünwald-panchromatic, marked R. A. L., or the May-Grünwald-Giemsa, marked Grübler, may be used. Other stains were also employed. Study of sections of the several organs is also highly important. Immersion in NaCl solution is unnecessary, but the same stains are used as for blood preparations. Various microchemic studies were made, as described. Hematogenesis for the adult and embryo, injections of various substances into the living animal, action of diastase on extracts of the various organs, and the cellular physiology were studied. The leukocytes consist of lymphocytes and monocytes identical with those of man. Hemacytoblasts, thrombocytes and immature lymphoid cells also occur. Granular cells, "explosive bodies," or "thygmocytes,"

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are merely lymphoid erythroblasts in a different stage of development. In the adult animal, the lymphocytes are derived from young microlymphocytes, microhemocytoblasts and microhemohistoblasts. In the early life of the embryo, all the cells originate from the hemohistoblasts. The leukopoietic structures consist of Cuénot's glands, the saccule, the connective tissue and the endothelium, all mesenchymatous. The blood-cells reproduce by amitosis. In general, they have the same biologic properties as mammalian cells. The thrombocyte probably influences coagulation. The article is prefaced by an historical review, descriptions are precise and complete and accompanied by very beautiful plates.

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**A Note on the Arneth Count in Malaria and Dysentery.**

*H. B. Newham and J. T. Duncan, J. Trop. Med. & Hyg., 24:301, London, Dec. 1, 1921.*

Contradictory results of the Arneth count in some diseases having been obtained by different investigators, the authors made their own normal standard. Selecting 6 healthy men who had never suffered from any serious disease, Newham and Duncan each counted 100 neutrophil cells in each subject, finally taking the mean of the two figures. The normal was finally fixed as between 240 and 260. Results of counts are recorded for tropical diseases found in 5 patients with benign tertian malaria, 1 with subtertian malaria (all 6 having parasites in the blood) and 4 with amebic dysentery in which *E. histolytica* was found in either the feces or scrapings of ulcers. Daily estimates were made of the index. Each did his counting independently of the other and counted separate films; the results were averaged. The conclusions drawn from a study of the 10 charts of the cases, are as follows: (1) That infection with *E. histolytica* causes no change of any moment in the Arneth picture. (2) That cases of malaria before treatment show a more or less definite shift to the left, but this rapidly gives way to a shift towards the normal as soon as the patient is vigorously treated with quinin, and the general toxemia is thus eliminated.

(1e—222)

(1e—222)

**Blood Counts with Oxalated Blood.**

*Nancy Yarbrough, J. Lab. & Clin. Med., 7:172, Dec., 1921.*

The author recommends that physicians whose work requires them to carry a patient's blood for some distance before counts can be made should carry a sterile 5 c.c. syringe and a sterile tube containing potassium oxalate dried in the hot air sterilizer. Four drops of a 20% solution will preserve 30 c.c. of blood. Blood drawn from the vein should be shaken for one minute with oxalate and then corked securely; complete counts can be made later. Tabulated results show that the figures for fresh and oxalated blood vary little. To assure accuracy the blood must be transferred immediately from the syringe to the oxalate tube, thoroughly shaken immediately and shaken again before counting.

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**The Biology of White Blood-Cells at Birth and during Infancy.**

*Max Frank, Ztschr. f. Kinderhk., 31:16, Berlin, Nov. 22, 1921.*

The preponderance of myeloid cells characterizes the leukocyte picture of the new-born. The normal change to the preponderating (Sec. 1—Page 382)

lymphatic blood-picture of the infant usually manifests itself on the third or fourth day and is generally completed in eight or ten days. This change of the myeloid into the lymphatic blood-picture was utilized by the author in order to gain an insight into the biologic relationship that has recently been claimed to exist between mononuclear cells and the lymphatic system. The author proceeds from the view that the constitution of the blood in the new-born belongs to the "syncainogenetic" phenomena (A. Kohn), which are produced in placentalia by symbiosis of the mother. The substances circulating in the mother's blood during pregnancy produce the same endocrinous changes in the child as in the mother. In the mother, as well as in the new-born child, a pronounced displacement to the left of Arneth's blood-picture takes place. That the change in the blood-picture is complete after one week in the new-born, while the other syncainogenetic phenomena persists much longer, would seem to be due to the fact that the blood is affected first and more strongly by changes in metabolism than the fixed tissue-cells.

The number of leukocytes decreases from the day of birth, with the exception of a brief period of increase about the fifth day. Concurrently the number of neutrophils decreases, and their initial strong displacement to the left likewise diminishes constantly. Only during the second stage does the number of neutrophils increase, and then only briefly, during which period a slight displacement to the left is observed. Obviously the initial displacement to the left is caused by irritation of the fetal bone-marrow by the mother's metabolic products. The disappearance of the latter leads to a cessation of the irritation. The second displacement to the left may be explained by assuming that, when the neutrophils diminish, the older forms are the first to disappear, leaving a larger percentage of younger forms behind. The total number of lymphocytes is constant so long as the myelogenous elements preponderate. Only the relative numbers fluctuate. An abrupt rise in the number of lymphocytes takes place only at the second stage of the leukocyte curve. Divergences from this normal course (initial decrease of lymphocytes, belated change of the blood-picture) indicate insufficiency in the lymphocytic apparatus.

The monocyte curve proceeds in a manner analogous to that of the lymphocytes, as regards absolute figures. During the initial period, in the monocytes, transitional forms preponderate over the granular round cells to a marked degree. Monocytes decrease in number only after the lymphocyte curve has attained the height which it maintains through infancy. The monocytes then reach a constant value and the displacement to the right in the monocyte-picture recedes.

From this Frank concludes that Bergels' view of the biologic relationship between the monocytes and lymphocytes receives support, and that an initial vicarious substitution of monocytes for lymphocytes seems to take place until the lymphocyte system attains its normal development. Frank finds two terminal forms of lymphocytes in the infant, one of which is characterized by a larger content of azurophil granules, while the other represents lymphocytic or lymphoblastic plasma-cells. About the fourteenth day (with displacement of monocytes to the left) the transformation of the blood-picture is complete. Frank is of the opinion that this stage may be defined as the end of the "new-born period." In practice, the blood-examination enables one to estimate the degree of maturity of the lymphocytic apparatus.

(1e—224)

**Leukocytes. The Basophil Corpuscles of the Neutrophils.**

*P. Weill, Arch. d'anat. micr., 18:46, Paris, Oct. 15, 1921.*

The material for study was obtained in Germany from about 100 cases of tuberculosis. Giemsa-Romanowski staining is not suitable. Hirschfeld's modification of Pappenheim's method, with a mixture of methyl green and pyronin, was found to give the best results. Staining for ten minutes in the oven is essential. The number of the corpuscles is variable, but constant for the same patient, examined for several days. Fever does not alter their morphology. Nothing can be stated concerning their function. The corpuscles are intracellular and stain bright red. Their outline is almost never regular, being unlike that of the granules of acidophilic or neutrophilic leukocytes. They have never appeared like round or oval droplets, but as irregular bodies, irregularly distributed throughout the protoplasm. Six or 7 may be contained in the same leukocytes, sometimes there is but 1, usually there are not more than 2. There is a certain resemblance to protozoan or spirochetal forms, but the corpuscles are never so clearly outlined. They appear to be secreted by the nucleus. Their fate is unknown. They are probably produced by a cellular lesion, which is not specific for any particular disease. They are probably not degenerative. A bibliography and plates are given.

(1e—225)

**Tryptic Action of Leukocytes Fixed by Alcohol.**

*G. Regard, Compt. rend. Soc. de biol., 85:1144, Paris, Dec. 17, 1921.*

The leukocytes were emulsified with a small quantity of physiologic solution, to prevent massive coagulation, and then fixed by 30% to 60% alcohol. The cells may thus be preserved for some time without losing their properties. Their form is maintained for two months. After a time, they become fewer and their structure is lost, especially those kept in 30% alcohol. The liquid thus produced has the reactions of leukocytes; placed in the incubator, it attacks cooked albumin, fibrin, casein and peptone, coagulates milk and liquefies gelatin. Strong alcoholic concentration destroys the tryptic power. The reactions indicated were carefully produced in separate tubes, arsenic sulphid being included among the substances affected by the alcoholic solution. The alcohol appears merely to slow the reactions typical of the leukocytes.

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**Appearance of Hemoglobin in Vertebrate Erythrocytes.**

*M. Prenant, Compt. rend. Soc. de biol., 85:912, Paris, Nov. 17, 1921.*

The manner of hemoglobin production in erythrocytes is not exactly known and general mitochondrial technic has been hitherto employed. Microchemical methods, with benzidin and hydrogen peroxid, are especially useful. Smears of bone-marrow are covered for some moments with a saturated solution of benzidin in physiological solution slightly acid (acetic); a drop of  $H_2O_2$  is added and the preparation examined under a cover-glass. In femoral marrow of an adult bird, mature erythrocytes are noted, stained uniformly blue, the compact nucleus being dark blue and a border still darker. In erythrogonia and erythroblasts, the nucleus is always stained more or less uniformly and  
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more or less deeply blue, according to cellular development. The cytoplasm contains fine, deep-blue granules, which have the appearance and location of chondriomes. In many cells, the cytoplasm is stained a general, pale blue, but sometimes nucleus and mitochondria are blue and the cytoplasm unstained; this fact excludes the hypothesis that hemoglobin simply condenses upon mitochondrial granules by adsorption. Sometimes the blue of the mitochondria even precedes that of the nucleus. At maturity, mitochondria cannot be differentiated by this method. The femoral marrow of a four-weeks' rabbit is similar. The nucleus is interpreted to be essential in hemoglobin formation, the latter appearing in the nucleus a long time before impregnating the general cytoplasm and while the cytoplasm is still very basophilic. Hemoglobin, and not peroxydase, is present in the nucleus; heating to 100° destroys peroxydases, but does not prevent staining. The chondriome is also a factor in hemoglobin formation. A peroxydase may be present, for heating destroys the chondriome and gives no evidence here. However, mitochondrial structures staining with benzidin and H<sub>2</sub>O<sub>2</sub> are relatively rare, and perhaps the chondriome contains hemoglobin. This explanation is more probable than Schridde's theory of mitochondrial origin. In birds, the nucleus becomes more and more homogeneous and loaded with hemoglobin. In mammals, this phase is followed by gradual paling of the nucleus, without expulsion or fragmentation, and merging into the cytoplasm. It seems impossible to believe that the chondriome entirely disappears. Although present in young erythrocytes and staining with benzidin, it cannot be detected in erythroblasts which are more developed but which still contain nuclei. Development of chondriome and nucleus are independent to a certain degree; the chondriome persists, but diffused hemoglobin covers it and prevents it from staining with benzidin.

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(1e—227)

**Structure and Laking of the Erythrocyte of Glycera.**

*M. Romieu, Compt. rend. Soc. de biol., 85:894, Paris, Nov. 17, 1921.*

Erythrocytes of *Glycera tesselata* (Grube) and *G. capitata* (Oersted) have been studied. Morphology is distinct and constant. They are disk-like, concave, with blunt and incurved edges. Viewed flat, they are circular; their concave opposite faces present a slight central projection, corresponding to the nucleus. Viewed obliquely, or when changing form, they are oval, quickly becoming bell shaped. The diameter in *G. tesselata* varies from 7-10 to 20-30 microns, the thickness being 4 or 5 times less. Color is yellow. The cells are contained within a distinct membrane, which readily stains with eosin, and is sufficiently elastic to permit temporary change of form; its contents are largely liquid. The nucleus becomes visible only by laking. Methylene-blue stains fine granules, but not the nucleus. The latter is spheroidal and irregular. There is a close nuclear network containing large, closely packed chromatin grains, causing a dark, compact appearance, quite unlike the nuclei of leukocytes. Amitosis has been observed. The addition of distilled water causes a change of form, first to bell shape, then to spherical, the nucleus becoming distinct and refractive; the cell contains fine, irregular, yellow granulations, the membrane appearing well defined and double. The intensity of the color diminishes, the contained hemoglobin diffusing through the membrane. The hemoglobin was

thought to exist simultaneously as a liquid and as fine, amorphic granules. The latter disappear when the cell is decolorized, a few refractive granules adhering to the cellular membrane, the cell appearing like a crystal globe containing the nucleus. The granules stain with methylene-blue and other basic stains after fixation, also with benzidin. Methylene-blue shows a sort of superficial reticulum, possibly comparable to the granulofilamentous substance of vertebrate red cells. The laked cell resembles the spherical, hemoglobinous figures described by Meves and Prenant. In a hypertonic medium, the cells become irregularly ragged and bossy, the latter causing the pseudopodic appearance mentioned by Goodrich. These cells may aid in interpreting phenomena occurring in the erythrocytes of vertebrates.

(1e—228)

**Influencing the Rapidity of Oxidation of Red Blood Corpuscles by Potassium and Radioactivity.**

*Philipp Ellinger, Hoppe-Seyler's Ztschr. f. physiol. Chem., 116:266, Berlin, Oct. 22, 1921.*

Potassium plays a part in maintaining the ion equilibrium in body fluids, and possess radioactive properties. It sends out beta and gamma rays, of which the former rays show especially great penetrating power. Bird blood-cells were used to determine the power of oxidation. Intact erythrocytes do not permit cations to pass, so that the rapidity of oxidation is practically uninfluenced by changes in the cation content of the medium. The bird corpuscles are washed in the centrifuge, allowed to freeze at  $-2^{\circ}$ , thawed, mixed with the examining fluid, and oxidizing power of the cell-suspension is determined by Barkoff's method. As controls, the same kind of blood-corpuscles were suspended in Ringer's solution, both with and without potassium. The glassware used was approximately the same size, so that the results read off in millimeters on the manometer were comparable, after correcting for the thermobarometer. Temperature of the hermostat was  $37^{\circ}$ - $39^{\circ}$ . The published tables show that the presence of potassium in the medium is absolutely essential for the oxygen respiration of the blood-cells. When the amount of potassium reaches a very low level, the oxidation power falls about  $1/3$ , while an increase in potassium raises it. It is undecided whether the influence of potassium depends upon the ion or upon the radiation. Potassium can be replaced by rubidium but not by cesium. The rays are not capable of replacing a lack of potassium. The emanation cannot accelerate the oxidation process. Fluorescin, even in small amounts, hinders respiration while eosin in small doses furthers, and in large doses hinders it. The furthering action seems to be independent of the potassium action, and immediate. It has not yet been shown that other radioactive elements can replace potassium.

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**On the Causes of Rapid Sedimentation of Red Corpuscles in Blood of Pregnant Women.**

*Tuda Sakae and T. Tsutsumi, Japan Med. World, 1:1, Tokio, Nov. 15, 1921.*

Since Fahraeus discovered that the blood of pregnant women shows more rapid sedimentation of red corpuscles than does the blood of normal women, the phenomenon has been considered one of the signs of  
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pregnancy. During the progress of experiments here detailed to determine the cause of the increased rate of sedimentation, it was also observed that the ratio of red corpuscles to plasma is greater in the blood of pregnant women, by an average of 1.52. This excess has a marked influence upon the rate of sedimentation, but when the ratio was reduced to the same as that of normal blood, there was still more rapid sedimentation. The next step in the experiments was to wash the pregnant blood corpuscles in physiological salt solution; this prevents the kinds of corpuscles from influencing the rate of sedimentation. The rate, however, was still higher in the blood in pregnancy. Studies of the specific gravity and viscosity of the serum of pregnant women show that they are lower than in normal blood. This is a contributory cause of the rapid sedimentation. But the difference is greater than can be accounted for by all the factors mentioned. In pregnancy, the corpuscles precipitate en masse; this facilitates rapid sedimentation and is interpreted as the second cause. The cause of the more easy agglutination of blood in pregnancy was found to be in the colloidal substances. The total amount of colloid had no influence, but fibrinogen markedly increased the rate; globulin also increased it; albumin decreased it. These results are due to the fact that these three colloidal substances are so changed in the blood in pregnancy. The concentration of hydrogen-ion is higher in pregnancy and may somewhat inhibit the rate of sedimentation.

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**Agglutination and Rapidity of Sedimentation of the Erythrocytes. II.**

*Wilhelm Starlinger, Biochem. Ztschr., 122:105, Berlin, Sept. 26, 1921.*

In an earlier report it was stated that the phenomenon of agglutination of erythrocytes, measured by the rapidity of sedimentation, depended mainly on albuminoid substances. In this connection, experiments were carried out to elucidate further the nature of the influence exerted by albuminoids, while the effects of lipoids were not taken into consideration. Inasmuch as the physico-chemical state of fibrinogen obviously influences certain reactions, different materials capable of affecting agglutination, such as kaolin, bolus alba and animal charcoal, were used in the experiments. These were designed to determine whether the disturbance in the mechanism of agglutination corresponding to the altered sedimentation could be detected by an altered behavior of albuminoids in the blood. The tabulated results show the decisive influence of fibrinogen on agglutination and in promoting sedimentation of the erythrocytes. Kaolin, bolus alba and animal charcoal (by absorbing fibrinogen) arrest these changes, which fact seems to be established by the reduction of refractive power and flocculation, as well as by the observation that no inhibition takes place in defibrinated blood.

By reason of their ability to promote agglutination and sedimentation, gelatin, agar and gum decreased the suspension stability of fibrinogen, whereas addition of highly dispersed decomposition products of albumin, in the form of tuberculins, increased the same. Elevation of temperature accompanying agglutination and sedimentation promotes hemagglutination, but if it is allowed to act previously, an inhibitory influence is manifested. Simultaneously refractive power and flocculation

are diminished. The inhibition of agglutination and sedimentation of the erythrocytes produced by addition of bolus, kaolin and animal charcoal may be explained theoretically (from observed experimental results) by assuming the liberation of the water soluble decomposition products of albumin previously bound to fibrinogen. The addition of tuberculins and the decomposition of albumin at a favorable temperature in the citrate plasma assist in the change. Conversely, the reduction of the suspension stability together with consecutively increased tendency to agglutination and speed of sedimentation brought about by gelatin, agar and gum, appear to be due partly to an alteration in the decomposition products of erythrocytes, and partly to the withdrawal of water due to swelling.

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**The Increase and Origin of Platelets.**

*Rinaldo Marchesini, Policlinico (Med. Sect.), 28:546, Rome, Dec. 1, 1921.*

The author takes issue with Perroncito who (*Haematologica*, 2: No. 3), described experiments in which he claimed to cause the reproduction of platelets. Perroncito treated the fresh blood of animals with sodium citrate and pyroдин, and found in forty-five to sixty minutes an increase of platelets that could not be attributed to derivation from white or red corpuscles. In a second experiment he studied a suspension of platelets and red corpuscles in plasma, under similar treatment, with leukocytes excluded. Here also he noted a great increase of platelets. He therefore concluded that platelets can reproduce themselves.

Marchesini replies that elements so maltreated could not possibly reproduce. He quotes his own experiments (*Policlinico, Pract. Sec. 1920, no. 8, p. 227*), with blood treated with osmic acid 1%, by which he was able to distinguish 3 conditions of red corpuscles, which he terms transitional (labile), semitransitional, and stable. The transitory were such as quickly lost their sarcoplasm and shrunk to the size of platelets, becoming so transparent as to be unrecognizable in uncolored solutions. If the defibrinated blood of a guinea-pig is thus treated, the transitional red corpuscles are not found; the semitransitional are constantly increased in numbers as blood changes continue, finally preventing an appearance of granular filaments variously disposed. They are evidently undergoing more slowly the same destruction that overtook the transitional forms. The multiplication of platelets observed by Perroncito is therefore to be charged to the semitransitional red corpuscles which, because of abusive treatment, become quickly altered, bringing to light the filamentary substance of the protoplasm—these changes being those of red corpuscles undergoing transformation into platelets.

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**The Derivation of Platelets.**

*Aldo Perroncito, Policlinica (Med. Sect.), 28:548, Rome, Dec. 1, 1921.*

Perroncito replies that Marchesini (in the foregoing) has misinterpreted him by putting together excerpts from his latest article in a way to make him say what he did not say. He refers the reader to his original article in *Haematologica*, 2: No. 3.

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1f. PATHOLOGY

(1f—16)

**The Pathologist as an Essential Factor in Clinical Diagnosis.**  
*John Harper, U. S. Naval M. Bull., 16:14, Jan., 1922.*

Microscopy is just as essential to clinical diagnosis as are auscultation, palpation and other methods of physical examination. There are here presented tables showing comparative clinical and pathological diagnoses made upon surgical tissue received at the U. S. Naval Medical School during the past two years. The service is responsible for diagnosis of considerable pathology of the female, especially that of the reproductive organs. It is noteworthy that out of 29 specimens of mammary gland examined, 12 were from male patients. Practically all pathology in the male breast is a benign fibro-epithelial tumor, carcinoma of the male breast being rarely seen in this service. Neoplasms averaged 40% of the total pathological conditions seen during this period, and of these, 43% were malignant. The greatest number of pathological conditions were gastro-intestinal. The organs or tissues requiring the most assistance from the pathologist in diagnosis were: the brain, salivary gland, jaw, lymph-gland, bone, mammary gland, testicle and omentum. When the surgeon made a positive diagnosis, he was correct in 57% of cases. Inflammatory conditions averaged 51% of the total pathology, tuberculosis comprising 15% of these. The pathological conditions which were most frequently undetermined or incorrectly diagnosed were: epuli (mouth), mixed-cell tumor (salivary gland), tuberculosis and malignant growths (omentum and mesentery), carcinoma (skin), benign fibro-epithelial tumors (mammary), lymphosarcoma and Hodgkin's disease (lymph-gland), benign connective tissue tumors, tuberculosis and malignancy in the testicle and in the brain, and tuberculosis of the bone.

(1f—17)

**Precipitates Produced by Fixation with Formol.**

*M. Fenger, Compt. rend. Soc. de biol., 5:1196, Paris, Dec. 17, 1921.*

In an examination of sections of lung, taken from new-born infants, with the view of determining the presence of meconium, precipitated masses were noticed which might readily be mistaken for meconium. These masses were situated within, or outside of, the alveoli. The tissue had been fixed in old formol, which had been prepared for several months, and which contained much formic acid. By neutralizing with decinormal soda, the precipitated masses were prevented from forming, or they could be produced at will by adding formic acid to neutral formol. In the presence of formic acid, hemoglobin is converted into acid hematin, or into hemochromogen, which oxydizes to hematin. The latter is insoluble in water, alcohol and dilute acids, but readily soluble in dilute alkalis. That formol may contain formic acid is well known; it is frequently kept neutral by adding sodium carbonate to the stock solution. The addition of 0.5 to 1% formic acid, by volume, is enough to produce the precipitated masses thus studied. Their extravascular occurrence is due to cadaveric hemolysis and penetration of hemoglobin into the tissues. No precipitation occurs if the specimens are fixed in the fresh state.

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**A New Method for Mounting Anatomic Specimens in Gelatin.**

*G. Brites, Compt. rend. Soc. de biol., 85:1172, Paris, Dec. 17, 1921.*

The usual method of mounting in Petri dishes is costly and applicable only to small specimens; the mounting is fragile and does not permit of easy examination. The author makes use of rather heavy copper bars. Two sizes are employed (44 by 1.8 by 3 cm. and 44 by 0.8 by 3 cm.; the respective weights are 2,025 and 880 gm.). Eight bars of each size suffice for ordinary needs. Of these bars, skeleton boxes are made. The specimens are mounted in a half Petri dish, in a watch glass or on an ordinary flat glass plate. They are surrounded by gelatin and the whole held together by plaster poured into the skeleton box. Specimens prepared by Kaiserling's process are best adapted to the mount thus described. Air bubbles must be removed from the gelatin by means of a hot needle. The plaster must not be entirely sealed about the box until the liquid appearing after solidification of the gelatin has been removed. Some hours are required for the solidification. The glass used for the background may be ground or colored. Remarkable effects are obtained by using blue or red glass. The plaster may be finally covered by paraffin, deposited by a xylol solution. The gelatin is used as suggested by Kaiser, i. e., by adding a few drops of formol at the moment of using. The formol prevents melting. The specimens may be small, or wide and thin. Color of the specimens will be preserved best by avoiding light and heat. Prepared by this method, specimens may be passed from person to person, as in class-room study, and are well suited for display in cabinets.

(1f—19)

**A Useful Variation from the Ordinary Method of Elective Staining of Fats with Sudan III.**

*Luigi Cevario, Riforma med., 37:1173, Naples, Dec. 10, 1921.*

The usual method has the disadvantage of dissolving part of the fats in the concentrated alcohol and so losing them from observation. The author has perfected a method for avoiding this difficulty: (1) To obviate the formation of precipitates in the alcoholic solution of Sudan III, he puts a certain quantity of Sudan I in a test-tube in a 30% solution of alcohol in distilled water, closes it carefully with paraffined cork and places it in a bacteriological stove at 37° C. for twenty-four hours, which causes solution of part of the Sudan. When a clear liquid is obtained, the reactions cut with the congelator microtome are placed in this and closed with paraffin. In eighteen to twenty-four hours, the coloration appears. After rapid differentiation in 70% alcohol, they are held in syrup of Apathj for one hour. But even at this point, the preparations are not always sure of interpretation. The author has accordingly stabilized the coloration en masse of the specimen with Sudan III, postponing the sectioning until the end. His technic is as follows: (1) Fix in formol 5%; (2) Rinse in distilled water; (3) Place in test-tubes in alcoholic solution of Sudan obtained as above; (4) Seal and heat at 37° C. for eighteen to twenty-four hours, maintaining liquid clear by adding ethyl alcohol, drop by drop if necessary; (5) Rinse the specimen now totally colored; (6) Section and place in distilled water. Rapid differentiation takes place in 50% alcohol, but this is often super-

fluous, for if the stain at the margins is heavy enough and not differentiated, the rest of the section has a delicate elective stain of the sudanophil substances alone, perfectly homogeneous and without precipitate. Comparing the stain obtained by the usual method and that obtained en masse, we find a greater quantity of sudanophil substances recognizable in the latter. Time is saved, and absolute homogeneity of stain is obtained, enabling the exact and constant valuation of the microchemical phenomena. The method is easy of execution, gives bright coloration and avoids numerous causes of error.

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**Chemical and Biochemical Researches on the Nervous System in Normal and Pathologic Conditions. IX. Pathologic Chemistry of the Brain in Diseases Terminating in Dementia Praecox.**

*Giacomo Pighini, Biochem. Ztschr., 122:144, Berlin, Sept. 26, 1921.*

This paper reports results of chemical analysis in degenerative diseases. The analyses and fractional extraction of nerve tissue were carried out in accordance with the methods of Mann and Koch, and Fränkel. In progressive paralysis, the brain showed percentage increases of water, cholesterin and protein substance; the unsaturated phosphatids were greatly reduced while saturated phosphatids, cerebrosids, sulphatids and sphingogalactosids were diminished.

In dementia præcox, water, cholesterin and protein were moderately increased; there was a slight decrease of unsaturated phosphatids, a marked decrease of saturated phosphatids, cerebrosids, sulphatids, and sphingogalactosids, and highly accentuated reduction of sulphur. In dementia pellagra, normal amounts of water and protein substance were found; there was a moderate diminution of cholesterin, more marked decrease of phosphatids, cerebrosids and neutral sulphur. In the cerebellum water, protein substance, and cholesterin were increased, while phosphatids, cerebrosids and sulphatids were diminished.

In general, it may be stated that these diseases lead chiefly to a degeneration of the true lipoids (phosphatids, cerebrosids), whereas cholesterin, water and protein substance remain unchanged. It is assumed that the newly formed molecules of protein take up a larger amount of water, which would compensate for the loss of lipoids. These researches, as well as the clinical data, apparently point to a similar terminal phase of dementia in all of these diseases.

(1f—21)

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**Examinations of the Speed of the Circulation in Experimental Anemias.**

*Moravetz and G. Denecke, Arch. f. exper. Path. u. Pharmakol., 91:37, Leipzig, Oct. 11, 1921.*

For the determination of the speed of the circulation, the authors used the method of Vorpahl. The animals were anesthetized with urethan and the blood taken from the right and left heart by puncture with a syringe containing 1 c.c. sodium oxalate and glass pearls. The analysis of the blood gas was made according to the method (ferrocyanid) of Barcroft Haldane. In preceding tests on normal rabbits an average loss of 5.17% in O<sub>2</sub> was found coinciding with the results of Vorpahl.

Anemia was caused by withdrawing blood from the ear vein; the  
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analysis was made immediately after bleeding. The average for the loss of O<sub>2</sub> in the circulation was determined as 3.1%, i. e., 60% of the normal; this is identical with the amount found by Bornstein with his CO<sub>2</sub> method. Thus it is possible to prove an acceleration of circulation in anemic animals. This acceleration increases conversely with the gravity of the anemia; comparison of the average figures, obtained for the loss of O<sub>2</sub> in normal and anemic animals, shows that the acceleration of the circulation may reach twice the normal, or even more in severe cases. Outside of this acceleration of the circulation a percentage increase in the efficiency of the oxygen present may act compensatingly in experimental anemias.

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**Adrenal Changes in Anemia.**

*S. Marino, Arch. di farmacol. sper., 31:154, Rome, May 15, 1921.*

This work covers changes in the adrenal medulla of dogs induced by anemia caused either by loss of blood or the introduction of hemolytic substances. Following the injection of such substances as acetylphenylhydrazin or tolulylendiamin vascular dilatation, with homogeneous fatty masses visible within the blood vessels was noted; perivascular lymphocytic infiltration in the space between the cortex and medulla; absence of karyokinesis; slight degenerative changes. There was found an increased amount of adrenalin, with a diminished production of chromaffin localized in some individual cells or groups of cells. Following repeated bleeding there was noted irregularity and faint staining property of nuclei; absence of karyokinesis; and an increase in chromaffin, more marked as more time elapsed after the last bleeding; the adrenalin content was variable. It would appear therefore that anemia, either from loss of blood or from poisoning, causes very little degeneration of the adrenal medulla. Furthermore, there seems to be no analogy between the chromaffin and adrenalin content, and one is compelled to conclude that these substances represent two distinct functions of the adrenal.

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**The Structure of the Human Hypophysis in Patients with Kidney Disease.**

*R. Hoppli, Frankfurt. Ztschr. f. Path., 26:22, No. 1, Wiesbaden, 1921.*

The author's work starts from an observation of Berblinger, who found in renal patients a striking increase of basophil cells in the anterior lobe of the hypophysis. The author made a study of the hypophysis in 45 cases which included kidney diseases of various kinds: parenchymatous degeneration, amyloidosis, tuberculosis, cystic kidney, acute and chronic glomerulonephritis, secondary contraction, arteriosclerosis. In all the cases, the neurohypophysis (neural lobe) and the pars intermedia showed no deviation from the normal, while in the anterior lobe, there was in 66.7% of the cases, an increase of basophil cells. For controls, 75 cases were taken which showed no greater kidney alterations than the above; in only 32% of these, was there an increase of basophils. To these cases belonged paralyses, changes in the endocrine glands, in the brain and its membranes. A study of age shows that the basophil increase does not belong to advanced age. Among the kidney-

cases the increase was lacking only in cases of parenchymatous degeneration in eclampsia. It was most evident in acute glomerulonephritis, but there was no constant relation between the kind of affection and the basophil increase. The same is true as regards blood pressure, nitrogenous residuum, cardiac hypertrophy, and appearance of uremia. Since the functional value of the basophil cells is not known, nothing can be said of the meaning of their increase in kidney affections.

(1f—24)

(1f—24)

**A Nodular Hepatic Lesion Containing Crystals.**

*J. Llambias, Compt. rend. Soc. de biol., 85:1207, Paris, Dec. 17, 1921.*

Yellowish granulations, 1 to 3 mm. in diameter, some of which were umbilicated, were noticed in the course of laparotomy done for hydatid cyst of the liver. The granulations were situated on the upper hepatic surface. A portion of the tissue bearing the granulations was removed and fixed in formol. Examination showed infiltration with polynuclears, lymphocytes and red cells. The nodule was contained within a fibrous capsule. The center was necrotic. In general, the section roughly resembled the usual appearance of actinomycetes. Fusiform crystals were present, especially in the center, but also to some degree in the periphery; these were 60 microns long and 8 microns thick. In section, they were hexagonal, with striæ at right angles to the principal axis. They were insoluble in acids, potassium hydroxid, alcohols, chloroform, ether, benzol and xylol. They stained feebly with eosin and picric acid, more strongly with basic stains (methylene blue and thionin), but without metachromasia, and took on a brownish tint with silver impregnation. The crystals do not seem to be inorganic salts, fatty acids or bilirubin. They are believed to be organic compounds, perhaps derivatives of uric acid.

(1f—25)

(1f—25)

**Parabiosis and Tumor Growth.**

*Isidor Kross, J. Cancer Res., 6:121, Apr., 1921.*

Kross started with the hypothesis that an animal immune to tumor inoculation possesses substances antagonistic to tumor growth or lacks elements necessary for tumor growth, and that these substances are present elsewhere than in the circulating blood. He assumed, further, that by performing a parabiosis between an immune animal and one susceptible to tumor growth, it might be possible to cause either the antibodies in the immune animal to cross over into the susceptible animal and make the latter also immune, or the substances favoring tumor development in the susceptible animal to cross over into the immune animal. To test these possibilities experiments were carried out with the Jensen rat sarcoma in 2 strains of white rats, one of which was known to be immune to inoculations of the tumor, while the other was known to be susceptible.

As a result of these experiments it is quite logical to conclude that parabiosis does not increase the susceptibility of the immune animal nor does it give immunity to the susceptible one, and that whatever the substances are that make for growth in the susceptible and for non-growth in the immune animal, these properties are not carried over by the parabiotic union. The lesser size of the tumor and the lesser rapidity  
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of its growth in the susceptible partner can be explained by the setback that the operation has produced and by the interference with the normal activities of the animal. It is unnecessary to assume that this phenomenon is one of partial artificial immunity similar to that produced by the injection of homologous tissue, since such immunity is known not to affect tumors after growth is begun but only to prevent inoculation. While the number of animals employed in these experiments is rather small, the results, taken in conjunction with those of other observers in this field, are sufficiently consistent to make it unnecessary to repeat them in a larger series.

(1f—26)

(1f—26)

**The Influence of Heredity in Determining Tumor Metastases.  
Studies in the Incidence and Inheritability of Spontaneous Tu-  
mors in Mice. Sixteenth Report.**

*Maud Slye, J. Cancer Res., 6:139, Apr., 1921.*

Slye, from her studies in the metastasis behavior of spontaneous tumors, reaches the following conclusions: In any given strain, the metastatic tumors tend to occur in exactly the same organs in which the primary tumors of that strain occur. In certain strains there is a tendency for tumors to metastasize in certain organs, whereas in other strains tumors of the same type in the same organ, even when they are of older and of larger growth, fail to metastasize into those organs. Leukemia and pseudoleukemia, occurring in tumor strains, infiltrate the organs which show the primary and secondary tumors of that strain. Tumors do not invade, even by extension, the organs from which primary and secondary neoplasms have been eliminated by heredity. Individuals with secondary tumors in any given organ seem to be as potent as individuals with primary tumors in the same organ to transmit, by heredity, primary tumors in that organ; therefore, heredity is a strong factor in determining where the secondary as well as the primary tumors of a strain shall occur, and also in determining what organs of a strain shall yield to the invasion of leukemia and pseudoleukemia.

The thing transmitted in the heredity of cancer is the tendency of an organ or organs to yield to cancer, and this is manifested whether the lesion is primary or secondary in that organ. The tendency to sarcoma, carcinoma, adenoma, etc., segregates out and is transmitted as such. A strong tendency to the location of one or more types of tumor in a specific organ or organs, such as the liver, kidney, pancreas, mammary gland, etc., is transmitted, owing to the segregating out of a peculiar type of tissue in these organs, which will respond in a neoplastic or leukemic manner to lesions of any kind which furnish a chronic irritation of not too destructive a type; that is, there is a specificity of tissue type, from organ to organ in a strain, which will make these organs react in a given way to a given type of irritation. It is, therefore, possible for ancestry to transmit to its posterity every possible combination of the neoplastic or leukemic tendencies which they carry either actually or potentially. This specificity of tissue type in an organ is found to be the nature of cancer heredity, and it is obvious that the nature of the response of such specific organ tissue is the same whether the lesion is primary or secondary in that organ. Heredity of a specific type or organ tissue is the fundamental influence in determining the incidence and location of secondary tumors and of leukemia and pseudo-

leukemia, as it is in determining the incidence and location of primary neoplasms.

Slye points out that any apparent testimony of the frequent occurrence of secondary tumors in man in tissues where primary tumors rarely occur is of no help here, as no human strain has ever been even partially analyzed, and no right conclusions regarding heredity can be drawn except from analyzed strains. She also suggests that until stocks of animals used in pathological and bacteriological experiments have been thoroughly tested out as to their inherited potentialities, such experiments will be lacking in any adequate control, since heredity is not considered although it is tremendously potent.

(1f—27)

(1f—27)

#### **Virchow's Theory of Irritation and Modern Experimental Tumor Research.**

J. Fibiger, *Deutsch. med. Wchnschr.*, 47:1449, 1481, Berlin, Dec. 1, 8, 1921.

A dyscrasia is never the immediate cause of tumor formation, but is simply the predisposing factor. Virchow considered metastatic nodules as the products of secondary deuteropathic dyscrasia, as a humoral contagion, or more rarely as a dissemination of cells (detached and transported portions of tumor). The frequent appearance of neoplasms on the lips, edges of tongue, anus, at narrow portions of the digestive tract, in undescended testicles, etc., indicates local irritation. Examples are given of the influence of irritation of various nature. Some of the most outstanding are striking, bumping (of testicles, central nervous system); physical, traumatic and chronic irritation (artificial limbs, pessaries, foreign bodies in tissue); melanoma in soles of feet of the negro, thermic irritation (Kangri-cancer in Cashmire—a receptacle filled with glowing coals is carried on abdomen,—cancer of skin of branded cattle, x-ray and other rays (mariner's cancer, in xeroderma pigmentosum); chemical irritation (in chewers of betel-nut, tar-cancer, cancer of bladder in anilin-workers); traumatic-chemical (pipe-smokers); saprophytes as tumor-producing; bilharzia cancer of bladder, trematodes in primary carcinoma of the liver; trichinosis in the human being, mites in chickens; bacteria, lupus, syphilis. The author succeeded in producing papillomas in experiments on animals by injecting various irritating substances. In a few cases cancer developed. In 1913 Fibiger described a procedure for the transplantation of nematodes to colored rats, and for the first time true, metastatic carcinoma was produced; the tumor-producing irritation of entozoa was proven. Later he again succeeded in causing malignant tumors by entozoa: a typical carcinoma by infection with spiroptera; and a typical sarcoma with cysticercus. In a third attempt he succeeded in causing eschars, inflammation and thickening of the skin by application of coal-tar to the skin of the back in white mice. Large keratoses, warts and papillomas also developed, and malignant tumors were noted at the base of these growths. The formation of carcinoma seems to begin early. Metastases were found here and there. Malignancy was verified by transplantation in several cases. By transplanting carcinosarcoma and continuing the process, pure sarcoma finally developed (the carcinomatous tissue was overgrown by the sarcomatous).

Carcinoma was produced in mice in Fibiger's laboratory by painting  
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with tar; carcinoma of the breast was produced by repeated injections of coal-tar products. All experiments confirmed the correctness of Virchow's theory of irritation. In spiroptera carcinoma, it is logical to assume some irritation acting directly upon the epithelial cells, and it may be assumed that this irritant is the product of excretions of the spiroptera. Virchow assumed a predisposition of the irritated tissues, either congenital or acquired, in regard to type and race. An especial predisposition of the connective tissue is to be assumed in the formation of sarcoma. The author does not altogether recognize this in regard to age and thinks that carcinoma occurs in older people because of a summation of the irritation in the later periods of life, more probable exposure to irritation at this time and the possibility that it takes a long time for the irritation to produce its effect so that the patients reach the older age before the effects manifest themselves.

Alcohol also plays at least a partial rôle. Bilharziasis carcinoma in the young is explained by the fact that the infection occurs, often, in early childhood. Loeb believes that the hormones of the endocrine glands may play a part in the predisposition as for example, the absence of certain protective hormones. The cells must have certain characteristics in order to react in the specific manner when irritation is present. It is not possible to determine the importance of metabolism, correlation of tissues and abnormal endocrine secretions.

(1f-28)

(1f-28)

**Virulence Artificially Increased Through Lactic Acid in Inoculation Tumors in the Mouse.**

*Paul Rostock, Deutsch. med. Wchnschr., 47:1323, Berlin, Nov. 3, 1921.*

Referring to Much's article in a previous number, Rostock experimented concerning the possibility of transferring, by means of lactic acid, increase of virulence just as apathogenic bacteria to the tumors in the mouse. These tumors are very significant for researches on experimental tumors, and highly virulent (100%) tumor stock is needed in experimenting with the biologic Roentgen dosage. Weichardt also pointed out the importance of lactic acid for the "unspecific" capacity increase, and observed that the effect of lactic acid with consequent neutralization (processes occurring likewise in intense fatigue) produces fusion products which "considerably increase" streptococcal growth. Through injections of lactic acid, the author succeeded in increasing the virulence of the tumors with reference to inoculation yield, rapidity of growth and metastatic formation. Without the addition of lactic acid inoculation, tumors lose considerably in virulence after several transferences.

It may be possible that tumor stock whose virulence is thus increased may help explain the still largely contradictory findings in researches on the immunity and therapy of the tumors in the mouse—provided that increase in virulence is also possible in tumor stock in the mouse other than that used in this experiment.

(1f-29)

(1f-29)

**Problems in Cancer Research.**

*Montrose T. Burrows, J. Cancer Res., 6:131, Apr., 1921.*

Burrows reviews the problems which it is intended shall be investigated  
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gated in the department of cancer research recently established at the Barnard Free Skin and Cancer Hospital, St. Louis. Of these the most pressing is the improvement in methods of diagnosis, especially of the diagnosis of internal cancer; another is the betterment of methods of treatment; and a third, and, of course, the most important, is the question of the etiology of the disease.

(1f-30)

(1f-30)

**A Study of a Lipomyxosarcoma with Comments upon the Origin of the Fat Cell.**

*Victor C. Jacobson, J. Cancer Res., 6:109, Apr., 1921.*

Jacobson reports a case of lipomyxosarcoma of the thigh of three years' duration. Careful microscopical examination of the tumor after its removal showed that it was composed of cells containing much fat, most of them of the embryonal type. Some of the cells contained both fat and mucin. Jacobson concludes that the fat cell and the fibroblast (the mucous connective tissue cell being considered as a modified fibroblast) are very closely related, and believes that his observations give support to the hypothesis that the fat cell is derived from the fibroblast.

(1f-31)

(1f-31)

**Septicemia: The Selective Deposition of the Colon Typhoid Group of Bacteria in Fixation Abscesses.**

*T. H. C. Benians, Brit. J. Exper. Path., 2:276, London, Dec., 1921.*

Seven experiments were undertaken to demonstrate whether the coli-typhoid group of bacteria can in fact pass out of the blood-stream into certain materials introduced into the subcutaneous tissues, and continue their growth there, while other bacteria present in the blood-stream fail to do so. The fixation areas were made with gum tragacanth. The emulsion of the gum was made with water, and a 5% solution of this was used. The migration of *Bacillus coli* (injected into the ear vein of a rabbit) from the blood-stream into a subcutaneous mass of gum in the flank was demonstrated within three hours. This experiment was repeated with *Staphylococcus aureus* instead of *B. coli* but no cocci were demonstrated in the gum puncture. Similar experiments using both *S. aureus* and *B. coli* were carried out and again it was shown that a definite selective capacity exists, which enables the bacteria of the colon type to leave the blood-stream and infect the gum much more readily than those of the staphylococcal type. Repetition of the previous experiments, using various other bacteria, resulted in the appearance of the coli-typhoid in the fixation gum almost always, while the *S. aureus*, *B. influenzae*, *M. catarrhalis*, etc., examined in the same way, almost invariably failed to be transferred from the blood-stream to the fixation area. When mucin, starch, etc., were used as fixation areas, positive results were obtained, but egg-albumin and fat gave negative results. It is suggested that the ready artificial infection of the mucoid bodies by the coli-typhoid bacteria bears a close similarity to the infection of the mucous membranes of the body from the blood-stream, as in the enteric fevers. In these experiments it was not shown whether the bodies of this physical character receive the bacilli owing to a selective mechanism or whether they merely favor their growth on account of the protection they afford. Phagocytes apparently did not effect the transportation of the bacilli.

(1f—32)

Influence of Adrenalin on the Course of Experimental Tuberculosis.

*Dario Maragliano, Riforma med., 37:1190, Naples, Dec. 17, 1921.*

The author studied the alterations produced in 40 guinea-pigs by the subcutaneous injection into the radix of the thigh of 1 c.c. of adrenalin hydrochlorate 1:1,000 together with human tuberculous material. The latter was injected 10 minutes after the adrenalin. In 12 other guinea-pigs adrenalin solution 1:4,000 was injected. Control guinea-pigs received tuberculous material without adrenalin. In the animals injected with adrenalin the most constant phenomenon was a considerable edema of the radix of the thigh reaching its maximum thirty to forty-eight hours after the injection. It was less noticeable in those that received the 1:4,000 solution, and did not appear at all in the control animals. Another striking feature was the frequency and extent of cutaneous necrosis, which was also lacking in the controls. The severity of the lesions bore no relation to the amount of material injected. Some animals developed abscesses or focal tuberculous nodules, the pus of which contained tubercle bacilli in 60% of cases. The author concludes that adrenalin in concentration renders the tissues of the guinea-pig more sensitive to the local action of the Koch bacillus. The chief practical purpose of the experiments was to learn whether the bacilli, finding the resistance of the tissues lowered by adrenal, had been able to invade the neighboring lymphatic glands. From fourteen to eighteen days after the introduction of tuberculous material and adrenalin there were signs of bacillary infiltration, in the controls as well as the other animals; hence it may be concluded that adrenalin does not produce an appreciable modification. As regards the length of time required for generalization of the infection, there was no appreciable difference. In another series of experiments the injections were made subcutaneously in the inguinal region, and the tissues bruised by Bloch's method to encourage lymphatic invasion. No difference of time was noticed in the appearance of the lymphatic tumefaction.

(1f—33)

Experimental Suppurative Typhoid Myositis.

*J. Sabrazès and D. Pauzat, Compt. rend. Soc. de biol., 85:1064, Paris, Dec. 10, 1921.*

Intramuscular injections of typhoid bacilli were made in the rabbit, at the root of the thigh. The material was taken from recent cultures on gelose, emulsion being made with normal saline solution. The muscles were infiltrated with pus after eighteen hours. Smears and sections were made. The muscle fibers had lost their striations and had become dissociated and fragmentary. Granular and hyaline degeneration were present, there was nuclear division in the sarcoplasm, and the sarcolemma was more or less destroyed. The leukocytes had penetrated between the fibrillary bundles. Other experiments have shown that muscular tissue is especially responsive to inflammatory reactions.

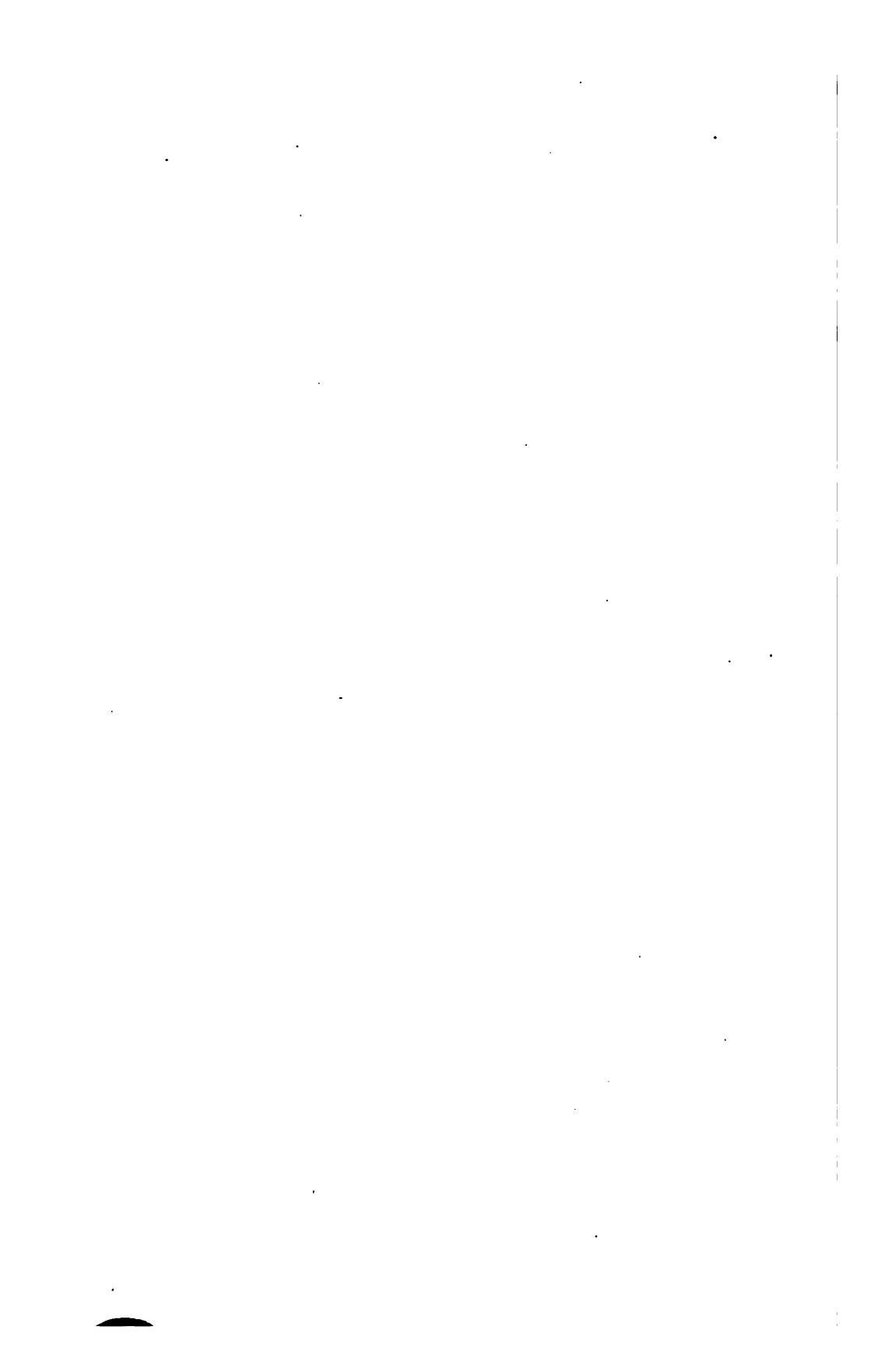
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**Ectasia of the Malpighian Bodies in Acute Typhoid Nephritis.**

*J. Sabrazès, H. Bonnin and R. Chandron, Compt. rend. Soc. de biol., 85:1065, Paris, Dec. 10, 1921.*

Nephritis occurs especially in epidemics of malignant typhoid. Observation of various complications of typhoid during the war, especially in natives of Annam, have particularly brought into prominence changes produced in the glomeruli. Pouch-like dilatations were formed from the vascular tufts. Sometimes the latter extended beyond the immediate glomerular region, being projected within the capsule of Bowman as sessile or pedunculate expansions. There was usually only 1 such expansion within a glomerulus, rarely 2, and the dilatations were not produced in all the glomeruli. Their diameter was 40 to 60 microns. They contained red cells, more or less desquamated endothelium and a thin collagenous border. Besides the usual lesions of typhoid, should be emphasized the alteration in the connective tissue of the tubules, vessels and glomerular capillaries, which is abnormally brilliant when stained with acid fuchsin or eosin, and which undergoes early hyalin degeneration. It is this loss of firmness which permits the vascular expansions within the glomeruli. These expansions have not the structure of aneurysms, nor should they be confounded with the hemorrhagic, glomerular cysts observed in experimental diphtheria. It cannot be determined whether this condition is peculiar to typhoid; it was found in one case of nontyphoid nephritis accompanied by extensive destruction of the tubules and glomeruli. The surviving glomeruli were hypertrophied and contained similar vascular expansions.



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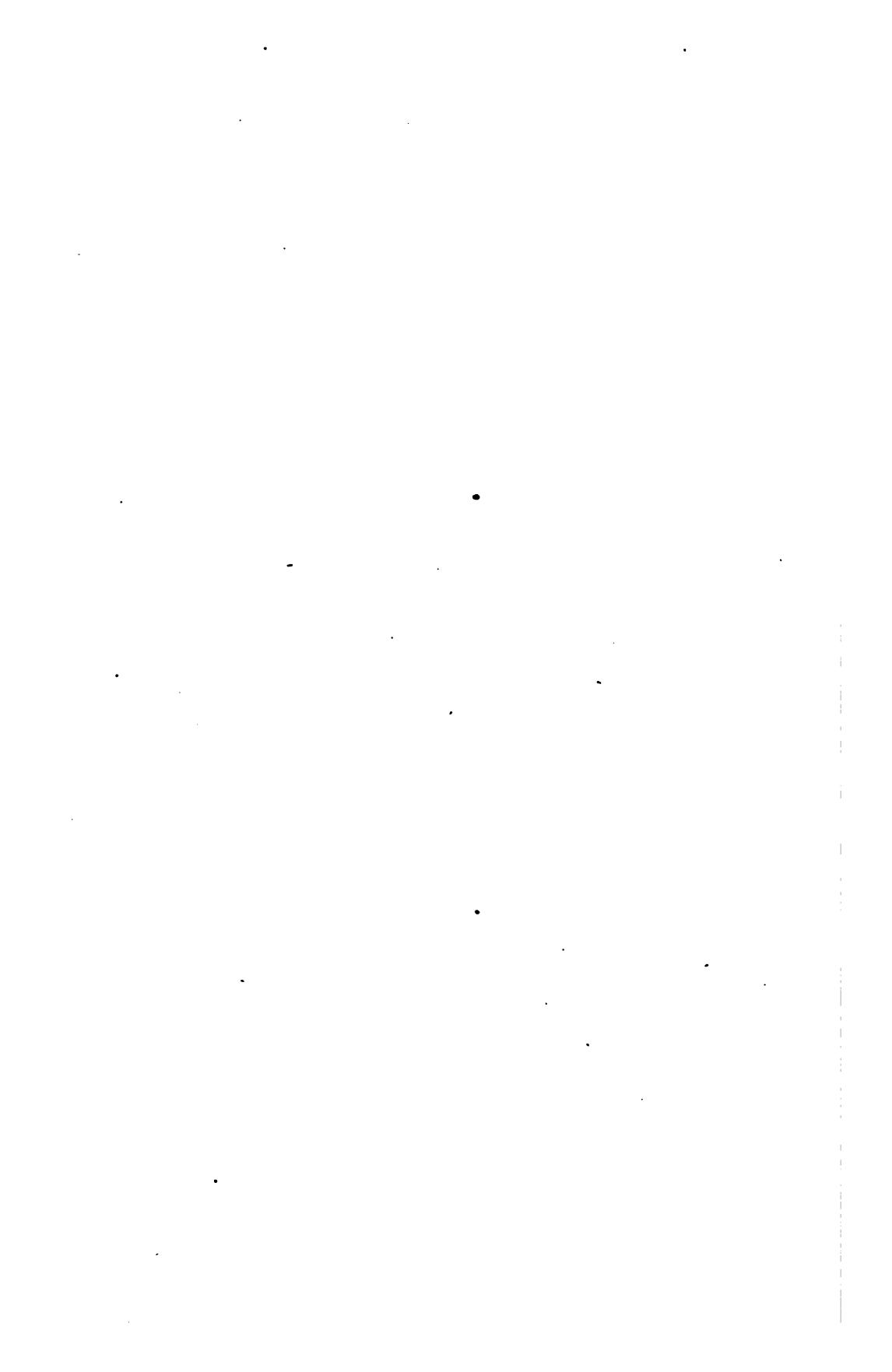
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## SECTION 1. ANATOMY, PHYSIOLOGY AND BACTERIOLOGY

### 1a. ANATOMY AND PHYSIOLOGY.

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Nature and the Occurrence of Spaces in the Mammalian Body.

Eberh. Ackerknecht, *Anat. Anz.*, 54:465, Jena, Nov. 30, 1921.

The author precedes his description of spaces by a discussion on the body cavities in mammals.

There are several varieties of cavities: (1) The preformed body cavities. They are closed and shut off from the outer world, and are lined with a layer of endothelium. They are related to the circulatory apparatus. Included under this head are the serous cavities, the arachnoid spaces, the joint cavities, tendon sheaths. (2) Cavities in direct communication with the outside; the content of these cavities, i. e., food, secretion, is not connected with their wall. They include the digestive tract, the urinary apparatus. (3) The cavities of the central nervous system.

As distinct from these body cavities the author designates as "spaces" those regions of the body through which nerves and blood-vessels take their course, pushing aside the surrounding structures. The walls of these spaces do not show a proper, continuous cellular lining. Their contents are soldered to the wall. The spaces can be classified from several points of view, according to function, and according to the relation between wall and contents. Among the second group are: (a) A cementing substance rich in fat unites the contents with the walls; in this way the contents are protected from injury, e. g., the orbit. (b) The contents are rigidly connected with the wall (umbilicus). (c) The contents glide along the wall (esophageal slit in the diaphragm).

Another grouping may be made on the basis of topographic anatomy: (a) Retroserous spaces, apposition of organs to serous cavities, e. g., kidneys. (b) Interserous spaces, lying between 2 serous folds, e. g., mediastinal space. The subpial space, which carries the afferent and the efferent vessels of the nervous system, also belongs to this category, as does the diaphragmatic muscle lying in the thoraco-abdominal interspace. (c) Superficially located fissures existing between the superficial muscles and fascias and the deeper organs. Among these are included the subscapular space, the popliteal space in man and in monkeys, the triangles of the neck. (d) Deep spaces which cannot be sharply limited from those of the preceding group. Among them are the epidural spaces of the spinal cord, the orbital space, the laryngeal aperture, the anterior thoracic space and the pelvic outlet, as well as the apertures for aorta, vena cava, and esophagus in the diaphragm. In addition to those described, there are a number of unnamed spaces, often filled with loose connective tissue and thus serving to conduct foreign bodies or disease organisms. All spaces are of great practical importance because of this characteristic.

(1a—138)

**Relations of the Hypoglossal, Vagus and Sympathetic Nerves to Fascia of the Carotid Artery.**

*P. Truffert, Bull. Soc. anat. de Paris, 18:429, Oct.-Nov., 1921.*

The author reviews the relations of the 3 nerves to the arterial sheath. The arterial and venous tracts are separate. The vagus is situated neither in the arterial sheath (carotid), nor in that of the internal jugular vein, but in the fascia uniting the two. The sympathetic is the only nerve essentially included in the arterial sheath. The location of the hypoglossal nerve is well known.

(1a—139)

**The Recesses Occupied by the Parotid and Submaxillary Glands.**

*P. Truffert, Bull. Soc. anat. de Paris, 18:429, Oct.-Nov., 1921.*

A dissected specimen is here presented showing the parotid situated in the subcutaneous cellular tissue, and not under the superficial cervical aponeurosis or in a fold of the aponeurosis. The parotid was lifted from its bed after simple removal of the cutaneous muscular layer. The superficial cervical aponeurosis, left intact, was readily observed to pass entirely under the gland. The preparation of the submaxillary gland showed its visceral bed, under the middle and superficial cervical aponeuroses.

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**The Vascular Sheath of the Subclavian Artery and the Suspensory Structure of the Pleura.**

*P. Truffert, Bull. Soc. anat. de Paris, 18:430, Oct.-Nov., 1921.*

The suspensory structure of the pleural vault is held to be closely related to the vascular arrangement of the subclavicular region. The vascular sheaths spread out in layers which follow the general direction of the branches of the vessels. These layers extend to the visceral terminations of the vessels. The structures here are similar to the vascular capsule of the thyroid. The subclavian artery and ascending branches from the arch of the aorta occupy the same sheath. On reaching the subclavicular fossa, the sheath is drawn outward by the arterial pedicle distributed to the upper limb. It is drawn forward and back by the costal arterial system, and thus constitutes a fibrous dome following the outline of the thoracic interior and extending above, and in contact with, the pleural vault. In the sheath accompanying the ascending branches of the subclavian are situated also the cervico-intercostal trunk and the thyrobicervicoscapular trunk. This sheath is drawn inward by the vertebral artery, toward the prevertebral aponeurosis; behind, by the cervico-intercostal trunk, toward the transverse process of the seventh cervical vertebra and neck of the first rib. It is continued above by the thyrobicervicoscapular trunk, toward the tubercle of Chassaignac. The sheath is reinforced along the course of the arteries and seems to be the same structure as that described by Sebileau. The suspensory apparatus of the pleura thus belongs to the vascular aponeuroses. It may seem unreasonable to regard such a distinct muscle as the suprapleural biceps as being dependent on a mere vascular sheath. However, it is well known that

muscles may be formed from the vascular tissues of the mesoderm. The author believes that the pleural muscular suspensor is so derived and that the scalenus anticus has a similar origin. The inferior ganglion of the cervical sympathetic is included in the arterial sheath. It is not located in the subretropleural fossa, but in its wall, behind the vertebral artery. The fossa contains only veins and lymphatics of the posterior scapular system. The fibromuscular suspensor of the pleura is not exactly inserted in the latter, from which it may be separated by cleavage. It fixes the cervical pleura as the endothoracic fascia fixes the parietal pleura.

(1a—141)

**The Nerve of the Fifth Visceral Arch and Its Relation to the Thyroid Foramen in Man.**

*Hans Dieterich, Anat. Anz., 54:398, Jena, Nov. 3, 1921.*

In addition to the typical nerves of the first 3 visceral arches, and the superior laryngeal nerve which belongs to the fourth visceral arch as the posttrematic nerve of the third branchial cleft, we find in the young human embryo a temporary fifth posttrematic nerve (the second posttrematic branch of the vagus nerve—Tandler). According to Grosser, this nerve may persist as the anastomotic branch between the external and internal branches of the superior laryngeal nerve. In such a case it passes through the thyroid foramen.

The author has studied a great number of embryos to determine the number of branchial nerves and the behavior of the nerve which passes through the thyroid foramen. Such a nerve was found in a number of the embryos examined but, from the study of the comparative anatomy, it can hardly be regarded as the nerve of the fifth visceral arch. In the Cyclodus, the nerve of the fifth visceral arch, the second branchial member of the vagus nerve, surrounds the fourth arterial arch from the back, as does the nerve of the seventh visceral arch, the recurrent nerve. The displacement of blood-vessels toward the caudal end of the embryo, in mammals, carries with it the recurrent nerve, and the same transposition should occur in the case of the nerve of the fifth visceral arch. This has never been observed. Hence the nerve of the thyroid foramen cannot be identical with the second posttrematic nerve; the former results from an anastomosis between the external and internal branches of the superior laryngeal nerve, while the nerve of the fifth visceral arch disappears completely.

(1a—142)

**The Snytopy of the Organs of the Upper Abdominal Cavity.**  
*Carl Rohde, Anat. Anz., 54:447, Jena, Nov. 15, 1921.*

In order to study the natural conditions of form, position and correlation of the organs in the closed abdominal cavity under the influence of functional activity, Rohde opened the abdomen of cadavers a few minutes postmortem, ligated the upper jejunal loop, filled the stomach and duodenum with about 100 c.c. 10% formalin solution, and the gall-bladder with hot paraffin; 100-200 c.c. 10% formalin were poured into the peritoneal cavity, the incision

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closed, and the cadaver hung up for at least twelve hours, to simulate the upright position. As long as the paraffin is hot, (about ten minutes) the organs can exert a mutual moulding effect upon one another. The impressions upon the liver differed in no way from those seen in the ordinary cadaver. But the fundus of the gall-bladder was flattened from apposition to the anterior abdominal wall. The undersurface and the sides of the gall-bladder are more or less compressed by the neighboring organs, according to the degree of their filling and their elasticity. The gall-bladder showed a colonic impression, and to the portal side of it, a duodenal impression. The broad hepatic ligament produces a more or less deeply marked furrow along the fundus of the gall-bladder. The side turned toward the stomach and duodenum shows impressions due to the extent of filling of these organs.

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**Two Casuistic Contributions to the Shape of the Human Stomach.**

*Curt Elze, Anat. Anz., 54:526, Jena, Dec., 1921.*

In the first case the cadaver was injected in the upright position with formol alcohol, the lungs being kept at a normal height by insufflation of air. On opening the abdominal cavity the dependence of the stomach's shape and position on the abnormally enlarged neighboring organs became apparent. The stomach was strongly kinked and displaced to the left and caudad, while its posterior wall was depressed by the pancreas.

In the second case (8 minutes after the execution of the individual in question) the stomach, which contained a little thin pap, was flat in the ventrodorsal direction, and showed no indication of an isthmus or of an antral pyloric sphincter. The interval between the greater and lesser curvature diminished gradually toward the end of the broad canal. Under the influence of cooling, equable contraction of the body and of the entire canal took place after one or two minutes, but even with this no contraction of the greater curvature was observed. The ventrodorsal diameter of the stomach increased. As a result of the latest researches the author has altered his views about the shape of the stomach and he now considers the canalis egestorius to be broader than he assumed heretofore.

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**The Choledochus Sphincter.**

*Felix Reach, Arch. f. exper. Path. u. Pharmakol., 91:170, Leipzig, Nov. 4, 1921.*

In the method hitherto employed by the author, a part of the liquid flowing from the burette through the common bile-duct into the duodenum frequently streamed back into the stomach. In the new experiments a drainage cannula was tied below the orifice of the bile-duct, whereby reflexes from the stomach, due to its fulness, were excluded. Such reflexes occur, also, in decerebrated (decapitated) guinea-pigs. No choledochus sphincter reflex from the intestine was produced by acid or alkaline solutions. Far-(Sec. 1—Page 404)

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dization of the lower extremities causes slight contraction of the sphincter, while the use of strong currents induces strong contraction of the same. Physostigmin sulphate in large doses (10 to 40 mg. per kilo animal body weight, subcutaneously) has a constricting action. Cocain hydrochlorid, intravenously in 10 mg. doses, and desalgin (a preparation of chloroform recommended for the treatment of cholelithiasis) in doses of 0.2 to 0.3 mg., have the same effect. Papaverin and scopolamin were found to be the only dilating agents.

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**Additional Cases of Plexus Formation in the Palm of the Hand.**

*S. Gehwolf, Anat. Anz., 54:435, Jena, Nov. 15, 1921.*

Supplementing a previous publication 5 more cases of palmar plexus formation are described: (1) The ulnar nerve splits at the pisiform bone into 6 branches, connected with one another by anastomoses passing over the volar arch. The fifth branch effects communication with the median nerve. (2) Plexus formation directly connected with the anastomosis between ulnar and median nerves. It is arched and forms the intersection point of fine nerve twigs, the longest of which again enters the anastomosis, surrounding in this course the trunk vessel of the second and third digital arteries. (3) Here also plexus formation in the region of the ulnar-median nerve anastomosis. Repeated intersection of the median and ulnar nerve fibers produces a fine-meshed network, through which passes the palmar arch and its branches. (4) Plexus formed almost entirely by the ulnar nerve. Three thick branches, undergoing extensive ramification, together with a few very fine nerve fibers form a dense network surrounding the palmar arch. One of the 3 main branches anastomoses with the median nerve. (5) Very fine nerve twigs form the plexus; they are derived in equal number from the ulnar and from the median nerve. Apparently, plexus formation is of very frequent occurrence; it is found in from one-third to one-half of all cases examined.

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**Topography of the Arteries of the Sciatic Nerves.**

*G. Chaumet, Heymann and Mouchet, Bull. Soc. anat. de Paris, 18:404, Oct.-Nov., 1921.*

The interfascicular distribution has not been clearly determined hitherto. Radiographic studies show that from its point of exit from the pelvis to its division in the upper part of the popliteal space, the sciatic receives 6 to 8 arteries. Their volume is not uniform. Two large, principal arteries join the nerve in the upper and middle thirds of the thigh. The others, or accessory arteries, are irregular. These vessels are supplied from the sciatic artery and the first 3 perforating arterics. They rarely originate directly, but usually from an intermediate muscular branch. They divide at the surface of the nerve into ascending and descending branches, the ascending being usually the larger. Collaterals are given off, likewise ascending and descending, dividing in the form (Sec. 1—Page 405)

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of a T. At the bifurcation of the sciatic nerve, the descending branch splits into 2 parts, supplying the internal and external branches of the nerve. In a third of the cases, each branch of the nerve is served separately by a descending arterial branch. A descending branch is usually distributed to each popliteal nerve. It gives off ascending and descending branches. Drawings made from the radiographic plates illustrate the arterial topography.

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**The Contractility of Human Skin Capillaries.**

*Walter Parrisius, Pflüger's Arch. f. d. ges. Physiol., 191:217, Berlin, Oct. 24, 1921.*

The experiments were carried out with the Zeiss skin capillary microscope, by O. Müller's method. They relate to peristaltic movements, spasms in vasomotor neurosis and the influence of adrenalin. Contractility of the capillaries is definitely determined, although the observations were made on morphologically altered diseased capillaries, so that it was not possible to say whether one was dealing with increased normal processes, or exclusively with products of the pathologic conditions.

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**Scale, Hair and Hair-Sheath in Mammals.**

*Miguel Fernandez, Anat. Anz., 54:506, Jena, Dec., 1921.*

On the basis of thorough embryologic and histologic researches on *Dasypus villosus* (peludo), the author discusses the relationship between the principal mammalian integumentary structures and their phylogenetic derivation. The most important of these structures are the scale (horny), hair and hair-sheath. Within the so-called "scale areas" (Pinkus) the following structures occur in this order: (1) the button, (2) the ridge, or true scale anlage, (3) bristles (and hairs, of which only the glands are preserved), (4) the bone-plate. In this research (4) is not considered, as it was probably acquired secondarily from the armadillos. The head is a lentil-shaped proliferation of the epidermis, below which the cells of the cutis are only slightly more dense than in the vicinity. Even with an embryo length of 63 mm. the cells formed by the stratum germinativum no longer participate in the building up of the button, so that it finally disappears. Initially it lies at the caudal end of the scale. In the later stages it does not lie so close to the caudal border of the scale and may even find its way to the cranial areas of the contiguous row of scales. The button is, therefore, a rudimentary structure, but as it occurs constantly also in other armadillos it is old phylogenetically and probably exercised an important function in the ancestors of the armadillo. The button is possibly homologous to the human hair-sheath, and in reptiles to those cutaneous sense organs (tactile spots) that lie on the caudal border of the scale. The first true scale anlage is represented by the ridge, which grows from the button in an anterior direction. It consists in an outward protrusion of the cutis over which the epithelium is thinner. It resembles the anlage of the reptilian scale. On both sides of the ridge, eminences are then produced. These

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lateral eminences are at first uniform structures. Later trumpet-shaped indentations appear toward the border and the hair rudiments are situated at the blind end of these. This surface relief can only be conceived to have been formed by the superficial extension of the scale and its growing around the hairs that stood originally to the right and left of the scales. At the border of the median field and the lateral fields, which are crenate through the ingrowing of the hairs, only glands are found later. The hairs themselves disappear entirely. In the same way, no hairs are found between the different scales in *Dasyurus peludo* but are found in *Dasyurus sexcinctus*, whose scales are narrower. But in older embryos, in the newborn, and in adults, bristles occur at the caudal end of the scales, which arise cranially from the button, as if they had displaced the button from the scale border by their growth. The author confirms the view previously expressed by Weber that the scale of the armadillos, and in reality that of all mammals, is homologous to that of the reptiles and descended from it. The button corresponds to a rudimentary reptilian cutaneous sense organ (Pinkus) but the hairs of the mammalian scale are also derived from these organs, viz., from those which in their position relative to the scale agree with the arrangement of the hairs. The hair glands are, however, new structures in mammals. The integumentary structures of every reptilian group from which mammals were developed may have had the following arrangement. The scales were rounded off caudalward and were supplied with a longitudinal keel. Below the caudal point of the keel was situated a particularly strongly developed cutaneous sense organ, from which the hair-sheath or the button sprang later. In the caudal and lateral borders of the scale were located small sense organs with distinct tactile bristles, which later became enlarged and transformed into hairs. This form of scale applies especially to the dorsal side; the arrangement on the ventral side and on the head was probably different.

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**Schultze's Caustic Soda-Silver Method for the Preparation of Axis-Cylinders and Nerve Cells.**

*Philipp Stöhr, Anat. Anz., 54:529, Jena, Dec., 1921.*

On Schultze's advice the author amplified the Schultze method. The treatment with silver nitrate is facilitated if the frozen sections are previously purified, i. e., the postmortem disintegration products, sediment, etc., are removed by careful washing with water, nitric acid or caustic soda (neutral acid and basic purification, respectively). The result varies with the nature of the purification, as each of these substances dissolves different forms of effete matter. The reagents required are (1) commercial formol, 10%; (2) normal caustic soda, 10 parts in 50 c.c. of distilled water (acid); (3) fresh solution of silver nitrate (to be used at most twice and for at least sixteen to twenty-four hours); (4) hydrochinon-formol solution (25 gm. hydrochinon, 100 c.c. distilled water, 0.5 c.c. commercial formol). The sections are placed in the solution diluted twentyfold. The reduction must always be controlled

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microscopically. This is followed by treating with distilled water, alcohol 96%, carbonylene, and balsam. For fixation with formol the sections must be as fresh as possible. Forty-eight hours after fixation with formol they may be cut with the freezing microtome. The directions are not entirely the same for different portions of the nervous system. For instance, the concentration of the silver nitrate solution is mostly 10%, but for the preparation of the glia it is better to employ a 0.5% solution and for staining of Purkinje's cells in the cerebellum a 0.25% solution. In these two cases caustic soda is also employed in a weaker solution. Much patience and accuracy are demanded in the application of this method.

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**External and Internal Migration of the Ovum.**

*Hanns Baur, Münch. med. Wchnschr., 69:48, Jan. 13, 1922.*

Five cases are published in which rabbits' ovaries were removed on one side and the tube ligated on the other side, and this was followed by pregnancy of the horn of the uterus of the side on which the ovary had been removed. In similar experiments Leopold found pregnancy in both horns of the uterus; all the ova for both horns must have come from the one ovary and they may have passed through each of the tubes into the corresponding horn of the uterus, in which case there must have been external migration from the oophorectomized side, or they may have all come through one tube into the uterus and part of them have ascended into the other horn of the uterus, as Leopold suspects (internal migration). In rabbits the two horns of the uterus open through separate cervices into a common vagina, so that in internal migration the ovum would have to pass these.

The author tried to settle this question experimentally, basing his work on Bischof's assumption that internal migration, if it is possible, would take place when one horn of the uterus received an abnormally large number of ova. As a rabbit gives birth to 3 to 8 young at a time, 6 embryos in one horn would be regarded as a maximum, and if more than that number of ova reached one horn they would certainly migrate if that were possible. In a series of experiments the author had uniform results. In spite of the fact that in 5 cases more than 6 embryos developed, not one migrated to the other horn, though such migration occurred with even smaller numbers in animals with a common cervix for both horns of the uterus. Internal migration can only occur when the ovum does not have to pass through the cervix. Leopold's experiments may be interpreted as meaning that external migration to the opposite side took place.

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**A Collection of Chinese Embryos.**

*Paul H. Stevenson, China M. J., 35:503, Shanghai, Nov., 1921.*

Stevenson presents this preliminary report from the Anatomical Laboratory of the Peking Medical College, to record certain data on the origin and early growth of an embryologic and teratologic collection of Chinese human embryos and fetuses. The (Sec. 1—Page 408)

nucleus of the collection, which today numbers 150 specimens, originated in the contributions of the medical men and women of Peking. Thus far 80% of the collection is from only 2 provinces, Chihli and Kiangsu. It is important that there should be a large number of specimens from a much wider area than is at present represented. The collection will lose its greatest opportunity for usefulness if it does not aim to constitute a source of reliable information on the peculiar racial characteristics of the Chinese as expressed in their embryologic development. The very early appearance in embryologic life, as well as the subsequent disappearance, of definite morphologic characteristics, often reveal genetic relationships which may be entirely lost to view in later stages of development. Upon this and other problems the collection will have its own evidence to present in the fulness of time. As is well known, the population of China, instead of being a homogeneous mass of people from a common stock, presents a racial pattern as complex as it is ancient. It is aimed to make the collection a standard for the study of all phases of the embryologic development of the Chinese, such as that of the Carnegie Laboratory of Embryology at Johns Hopkins Medical School is for the whites and blacks of America. Although the collection has not yet attained sufficient size to provide enough specimens of any one type for the study of specific problems, yet some work has already been done. Dr. Cowdry has begun several interesting studies on the development of the various internal organs in successive fetal stages. This work is incidental to, and in preparation for, a larger work on the endocrine glands. Casts are being made of all the specimens in order to preserve a record of the external form of each. Some of the larger and more fundamental problems yet to be worked on are outlined, and an appeal is made for more specimens. There is appended a complete list of the specimens, of which 25, or about 16%, are either pathologic or abnormal.

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**The Relation of the Lateral Line Organs of *Necturus* to Hearing.**

*W. J. Paul Dye, J. Comp. Psychol., 1:469, Dec., 1921.*

Although aquatic amphibians possess lateral line organs, their reactions to sounds have not been studied. This paper describes experiments carried out for purposes of testing the function of the lateral line organs of the mudpuppy in relation to slow vibrations in water. The results indicate that the lateral line of the mudpuppy serves the same function in aquatic amphibians that it does in fishes. Observations were made which appear to indicate the length of time required for the establishment of connections with the lateral line organs after the nerves had been cut. The animals in which the lateral line nerves had been cut were subjected to the tests at intervals of two days. About the eighteenth day from the time of operation, doubtful responses were noticed. On the twenty-first day the animals responded as before operation. This indicates that regeneration of the connections had occurred and also

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gives further support to the view that the lateral line system is important in the discrimination of sound vibrations.

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**Studies on Bioluminescence: XIV. The Specificity of Luciferin and Luciferase.**

*E. Newton Harvey, J. Gen. Physiol., 4:285, Jan. 20, 1922.*

Harvey submits a tentative classification of the various types of luminescence found in living things and, in connection with this data, discusses the luciferin-luciferase reaction and the specificity of luciferin and luciferase. Luciferin is made by adding hot water to the luminous organs of the animal or by quickly heating the luminescent extract of the luminous gland to temperatures which permanently quench the light, or to boiling. By this means the luciferase is destroyed on heating before the luciferin (which is not destroyed by heating) has been completely oxidized. Luciferase is prepared by allowing a cold water extract of the luminous gland to stand until the luciferin has been completely oxidized.

Among the 16 groups of luminous forms investigated by the author, in only 4 (fireflies, pholas, ostracods, and odontosyllis) was it possible to demonstrate the luciferin-luciferase reaction. In many groups this might have been due to the small amount of these substances present in the luminescent organism or to their instability. Concerning the specificity of luciferin and luciferase the author made a study of the luminescence resulting when Cypridina luciferin and luciferase was mixed with these bodies prepared from other animals of all degrees of relationship as regards Cypridina. From the tabulated results the author concludes that these 2 substances responsible for the production of light by Cypridina are specific to the highest degree.

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**Observation and Depiction of Thin Strings.**

*W. Einthoven, Pflüger's Arch. f. d. ges. Physiol., 191:60, Berlin, Oct. 24, 1921.*

The visibility of thin strings as luminous ones against a dark background, and as opaque ones against a bright background, is of great theoretic and practical interest. They find practical application in the string galvanometer. On a dark background 0.1 threads are seen easily; they may be fastened, crossed, strung in the galvanometer. Every string, even the thinnest, can be rendered visible ultramicroscopically, so long as it is possible to bring it under the microscope. The diameter of the thinnest visible string is calculated by means of certain optical considerations to be  $0.2 \times 10^{-6}$ , so that the diameter of a hydrogen molecule would be a million times larger. The visibility of a dark string against a bright background does not depend on the dimensions of the retinal elements, but on the capacity for distinguishing 2 different brightnesses. Two separate lines (light lines) can just be seen as separate lines at a visual angle of 60 sec., while a string is visible even at an angle of 2 sec. Every factor that renders the microscopic picture of the bright string against a dark background less sharp

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increases the apparent string diameter. The string diameters obtained by microscopic measurement and designated by 0.1—0.2 are either correct or too large, as the microscope is not an ideal instrument. The conditions for the visibility of a dark string against a bright background were then examined. Strings of a diameter of 0.2 are pictured sharply in contrast when the projection objective has the aperture 0.95, so that small irregularities are still separately visible. Presumably, strings with diameters of 0.03 or 0.04 should be made visible by the objectives on the market and a photogram of an atomized quartz string led to the assumption of visibility of such a diameter.

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**Humoral Transfer of the Effects of the Cardiac Nerves.**

*O. Loewi, Klin. Wchnschr., 1:22, Berlin, Jan. 1, 1922.*

The author isolated the heart of a cold-blooded animal, filled it with Ringer's solution and electrically stimulated the vagus and accelerans. He then removed the Ringer's solution from the isolated heart and put it into another and fresh heart. The effect on the latter was the same as though the vagus and accelerans were stimulated electrically. Substances, therefore, must remain in the heart after stimulation of the nerves, which correspond in some way to the form of nerve stimulation. These substances are the result of influences of the stimulation of the nerves and are not products of the cardiac muscle, which has undergone changes as a result of effort under the influence of stimulation of the nerves. This is proved by the following experiment: The effects of vagus and accelerans action are seen one after another after common stimulation of the trunk containing vagus and accelerans fibers in the hearts of toads. The same effect is obtained with the contents of the heart, even though the vagus alone was stimulated. The substances must be formed as a result of stimulation of the nerves and before there is a chance for the appearance of the mechanical results of the stimulation. These substances are organic in nature and represent hormones which are formed locally and which are effective.

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**The Alternans Problem.**

*S. de Boer, Pflüger's Arch. f. d. ges. Physiol., 192:183, Berlin, Nov. 12, 1921.*

Ventricular alternans may be produced with practical certainty in a dehematized and suspended frog's heart by warming the sinus venosus for a short time (syringing with a 0.65% solution of common salt at 25-30° C.); during the process of cooling down, the same high ventricular systoles return. Electrocardiograms obtained at the same time show complete ventricular electrograms during the large systoles, but, during the small alternans systols, only the basal component is found, the apical being lacking. The ventricular apex does not contract during the small systole, but contracts very strongly during the large systole (partial hypersystolia). The alternans is produced by a disturbance of the meta-

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bolic equilibrium of the ventricular muscle, in consequence of increased frequency, which shortens the time available for restitution. This disturbance of the metabolic condition is necessary for the genesis of the alternans.

This disturbance may also be produced by poisons inducing increased activity of the ventricular muscle, such as digitalis, veratrin, or barium chlorid. Here again, partial asystolia during the small systole is noticeable, the uncontracted apical portion being protruded in the shape of a hernia, by the action of the blood which is forced in. A retardation of the conduction of the stimulus may also produce the small ventricular systoles which are observed following digitalis poisoning, as well as after an artificial extrasystole. These processes are influenced, above all, by the duration of the ventricular pause, which is great after small ventricular systoles and small after large ventricular systoles. After the longer pause, the metabolic condition of the ventricular muscle is improved, and the normal rhythm is preserved. The temporal relations between the ventricular pause and the residual refractory stage of the ventricle are of decisive importance. In this way, the ventricular alternans forms a transition from the normal ventricular rhythm with equally high systoles to the halved ventricular rhythm. Before the transition to the ventricular alternans, there is a decrease in the contractility and in the rapidity of the conduction, and an increase in the duration of the refractory stage, which is an expression of the deterioration of the metabolic condition. In this condition, the alternans is more favorable to the general metabolic condition of the ventricular muscle than is the normal rhythm, and the same is true of the halved rhythm. Ventricular alternans must also be assumed in the case of pulsus alternans, without exception; it is not sufficient to base it exclusively upon hemodynamic conditions.

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**The Mode of Action of Potassium Upon Isolated Organs.**

*A. J. Clark, J. Pharmacol. & Exper. Therap., 18:423, Jan., 1922.*

Zwaardemaker has claimed that the presence of potassium is essential for the maintenance of the function of isolated tissues, because of its radio-activity, and that potassium can be replaced in Ringer's fluid by other radio-active substances in equi-radio-active quantities. When an isolated frog's ventricle is arrested by lack of potassium, the introduction of small traces of radio-active substances will cause it to resume an automatic beat. Zwaardemaker concludes that in a large number of systems the potassium atom may, as regards function, be replaced by all the other radio-active elements, provided that the doses are equi-radio-active; that any radio-active element added in a dosage equi-radio-active to potassium, to a potassium-free Ringer's mixture, renders such a solution as effectual a circulating fluid for the heart of a cold-blooded animal as the original fluid. The writer carried out experiments with isolated frog's heart, and studied the changes which occurred when potassium-free Ringer was substituted for normal Ringer's fluid, comparing with these the effects of replacing normal Ringer by

Ringer minus potassium but with radio-active substances added. He found that, although uranium will excite a heart which is arrested by lack of potassium, it cannot be said to replace potassium in the manner in which rubidium will replace potassium. Zwaarde-maker has replied, stating that failure to obtain positive results with uranium was due to using too high a concentration of potassium in the normal Ringer's solution.

The present experiments of the writer represent a further attempt to determine to what extent potassium can be replaced by rubidium and cesium and by the heavy radio-active metals uranium and thorium, in solutions which are used to preserve the activity of isolated tissues of frogs and mammals. He found that rubidium acts as a perfect substitute for potassium in all of the isolated tissues examined; cesium acts as an imperfect substitute; thorium and uranium do not act as substitutes for potassium, but as irritants to the frog's heart, inducing automatic beats in hearts arrested by lack of potassium.

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**Polar Excitation and Inhibition in Arteries.**

*Paul Liebermann, Pflüger's Arch. f. d. ges. Physiol., 192:130, Berlin, Oct. 29, 1921.*

The arteries of the web of a frog may be examined independently of the variations of excitability in the denuded organ; they also are under permanent pressure from within, so that any relaxation is bound to become visible as dilatation. The cathodal contraction and anodal dilatation of the arteries is effected with great distinctness; the former may reach the degree of occlusion. No influence is observed on the veins. The latency increases in regard to both effects as the intensity of the current increases. Both effects are of a permanent character if the current is not too weak even though the cathodal constriction gradually decreases a little. If the intensity of the current is great, the cathodal effect increases rapidly, and slowly if it is less considerable, so that, if the current is of short duration, an increase of the cathodal constriction may be observed even after opening of the circuit. On cessation of the stimulation, cathodally constricted arteries dilate, whereas anodally dilated arteries contract. In the state of strong dilatation by other stimuli, the polar excitations are inefficient. The cathodal constriction is restricted to the vicinity of the electrode, whereas the anodal dilatation is propagated into the capillary ramifications. However, this is not a case of essential differences between the poles, but of the effects of the unipolar arrangement, which gives rise to virtual poles.

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**The Reaction of the Capillaries to Mechanical Stimuli in Pregnant, Nonpregnant and Puerperal Women.**

*Ernst Lennartz, Pflüger's Arch. f. d. ges. Physiol., 191:301, Berlin, Oct. 24, 1921.*

The researches were carried out on the nail-groove with the Leitz binocular microscope. The capillary flow shows varying  
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velocity but no pulsations corresponding to cardiac activity. Stases and reverse flow are observed. Stases are rare in nonpregnant women, but frequent in pregnancy, and increase toward the time of childbirth. In puerperal women they are found only in isolated cases during the first days after childbirth. In the pregnant, longer loops with dilated venous stem are formed. The stimuli employed were stroking, rubbing, squeezing, pricking and scratching. The reaction differs locally and individually (appearance of new capillaries on the arm but not on the nail-groove). After irritation the stases disappear and the bluishred coloration is replaced by a bright red one. As a result of 12,000 observations on 25 pregnant women, the average duration of the stases was found to be 737 sec., i. e., 6.14%, after irritation 257 sec. or 2.97%, corresponding to a reduction of 51.6%. Irritation also increases the velocity of flow and produces dilatation. In the case of nonpregnant and puerperal women the effect of irritation is not nearly as distinct but it is marked in patients having cold hands and granular capillary flow.

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**The Salivary Secretion.**

*Arthur Scheunert and Alfred Trautmann, Pflüger's Arch. f. d. ges. Physiol., 192:1, 33, 70, Berlin, Oct. 29, 1921.*

*Parotid secretion in the horse.*—The generally established laws of salivary secretion were derived from observations on dogs and partly verified with regard to man. But nourishment and absorption of food are different in the case of herbivorous and omnivorous animals; and in some of them (ruminants), saliva plays a special part. The question is whether, in these animals, the same conditioned reflexes are the decisive factors as in the case of dogs. An unambiguous decision can only be arrived at on the basis of a simultaneous histologic examination.

In the horse, the parotid saliva, during chewing, issues from the papilla and is transferred to the outside in squirts, if the fistula is permanent, whereas it flows continuously, if the fistula is temporary. There is no psychic secretion; for that reason olfactory stimuli are inefficient. The principal part is played by mechanic stimuli; chemical stimuli are of very secondary importance.

On the side where the chewing takes place, the secretion is more active, with a higher percentage of ash and chlorin, and a lower percentage of nitrogen. There is no specific adaptation to the food. The parotid saliva does not contain any diastase. In the case of unilateral fistula, the secretion of the side which has been operated upon is lacking. Preference is given in chewing to the intact side. The absorption of food is retarded, deglutition is rendered more difficult. The parotid fistula undergoes morphologic transformations in the course of its progress, the normal terminal parts becoming finally involved in connective tissue hypertrophy.

*Secretion of parotid and mandibular glands in sheep.*—Fistulas of the parotid and mandibular glands were made upon 11 animals. In the case of sheep, the parotid gland secretes continually (4-5 c.c. in ten minutes); abolition of the secretion of only one gland

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leads to the omission of rumination and of the regular absorption of food and, in consequence, to cachexia and death. The permanent secretion is for the purpose of moistening the contents of the 3 antestomachs and the neutralization of the acids of fermentation. Its product is strongly alkaline, and, during the absorption of food, it takes place somewhat more rapidly and with a higher percentage of alkali. Psychic secretion is slight. The secretion of the mandibular gland takes place only during the absorption of food; its product is neutral or slightly alkaline, and mucin is present. Here again, psychic secretion is of a slight character. An influence of the quantity and quality of food is not to be observed in the sense of specific adaptation. Both the parotid and the mandibular gland were of a pallid appearance and showed decrease of weight after fistulization. In the mandibular gland, transformations appeared after the fistula had been in existence for some time. They were in the nature of proliferation of the supporting tissue (effacing the lobular character), decrease of the marginal cell complexes, diminished susceptibility to staining. The parotid glands also exhibited symptoms of permanent excessive irritability (conditions of irritation), leukocytes being present in abundance.

*Conclusions.*—In regard to the stimuli of secretion, there is a difference between horses and sheep, in that psychic secretion is to be observed only in the case of latter, slight though it be. The acute sense of smell of the horse serves for the examination of food as to its suitability. It is not possible to establish any quantitative relations between the quantity of saliva and the absorption of food in consequence of the variability of the secretion. Nor is there any direct relation between the maxillary movements and the glandular activity. The quantity of efficient mechanic stimulation varies in accordance with the intensity of the movements and the quantity of chewed food. The excitation of the glandular function seems to start from certain mucous membranes, as is suggested by the preference of the side on which the chewing takes place with respect to secretion, the effect of the probing of the excretory duct, and the inactivity of the mandibular gland in ruminants in which the incisors and the region of the mucous membrane containing the excretory duct do not take part. There is no characteristic adaptation of the saliva to the various kinds of food, contrary to the expectations engendered by Pawlow's doctrines. Permanent fistula is succeeded by transformations of the glandular structure, the diversion of the secretion to the outside, resulting in a decrease of the weight of the gland and in typical connective tissue degenerations. The latter were also observed in dogs. A historic control examination is therefore indispensable, for the interpretation of secretory phenomena on the basis of experimental fistula, if any laws are to be established in regard to quantitative and qualitative variations of the fistula secretion.

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**Physiology of the Liver. IV. Condition of the Liver During Feeding with Protein After Previous Feeding with Glycogen.**

*P. Juunkersdorf, Pflüger's Arch. f. d. ges. Physiol., 192:305, Berlin, Nov. 12, 1921.*

After hungering four days, the dogs were fed on glycogen for three days, and during the three following days, received protein in the form of beef or cod fish. The increase of the body weight during the period of protein feeding is not always paralleled by a corresponding increase in the weight of the liver. The amount of glycogen contained in the liver is surprisingly low; it is therefore to be supposed that the mechanism of the liver was injured by the exclusive feeding with protein. The same is true in regard to the glycogen contained in the muscles. This is to be accounted for by the effect of unphysiologic products of protein decomposition (Asher's liver poisons). The amount of fat contained in the liver is increased, which makes it appear probable that the liver glycogen is transformed into fat by the liver-cells themselves. All this proves once again that the function of the liver is considerably influenced by the quality and quantity of the food consumed as well as by the manner of its administration. This accounts for the individual differences in the size and the chemical constitution of that organ. Inappropriate nourishment and, above all, a sudden transition to unaccustomed nourishment, may result in considerable functional disturbances and, consequently, in phenomena of irritation and abolition. The fact that the unphysiologic products of protein decomposition injure the structure and function of the liver-cells tends to support, on the one hand, the theory of normal decomposition down to the amino-acids, and, on the other, the possibility of the resorption of products of digestion of a higher molecular constitution.

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**Some Human Digestion Experiments with Raw White of Egg.**

*Mary Swartz Rose and Grace MacLeod, J. Biol. Chem., 50:83, Jan., 1922.*

The authors conducted experiments on 10 subjects, all healthy young women, who took daily from 10 to 12 whites of eggs as a part of a simple mixed diet, first cooked, in a three-day period, then raw for the same length of time. The diet was uniform throughout the experiment and furnished 67 gm. protein, to which the egg whites contributed 48 gm. The experiments were divided into 3 groups, one in which the raw egg whites were taken thoroughly beaten, one in which they were taken in their natural state, and a third in which half were beaten and half unbeaten. In no case did any one of the subjects show any signs of indigestion. Coefficients of digestibility were calculated for the total protein of the diet and also for the egg protein alone. The results show that the cooked eggs were uniformly well digested, coefficients ranging from 83 to 91% with an average of 86% for the diet as a whole; or from 82 to 93% with an average of 86% for the egg white alone. On the whole the raw whites were well utilized, the authors found, the

average difference between the cooked and raw being only 4% for the protein of the whole ration or 5.5% for the egg white protein alone, in favor of the cooked. The differences between the cooked and the raw whites varied with the mode of preparation, those beaten light being the best utilized, and those taken in the natural state least well absorbed.

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**Nitrogen Assimilation on Animal and Vegetable Diet.**

*L. Dienes, Biochem. Ztschr., 123:128, Berlin, Oct. 25, 1921.*

According to the results of different investigators, the albuminoids of potatoes and of bread, both of which have approximately the same low values, produce an equilibrium of nitrogen when used over long periods. Starting upon the assumption that a difference in the behavior of individual albuminoids—if such differences exist at all—would be most noteworthy when using large amounts of albuminoids, the writer investigated the assimilation of albumin after it was preceded by an intensive loss of albumin matter, serving it in one foodstuff exclusively. The person upon whom the experiments were undertaken was a healthy man of 25 years, who on account of corpulence had gone through a treatment which had reduced his weight from 104 to 86 kg. This was followed immediately by the first series of experiments undertaken in the following manner. The minimum of albumin of the person was first determined, in order to have a basis of comparison for the amounts of albumin consumed and assimilated. Further experiments were undertaken to determine the assimilation of albumin first on low, and later on increased rations. It was desired to compare the assimilation in the case of meat, bean, and wheat diet. A second series of experiments were undertaken to control the figures obtained for wheat. The individual periods lasted five to seven days. The caloric value of the foodstuffs attained the average required. The nitrogen content of the foodstuffs was determined by Kjeldahl's method, the dry substance by drying at 100° C., and the amount of fats by the Liebermann-Szekely method. The same determinations were made for the excrements, but in this case the amount of starch was determined through saccharification with a 2% solution of hydrochloric acid. The results of the investigation show that after intense emaciation greater amounts of nitrogen are assimilated on animal diet than on vegetable diet (consisting mainly of wheat) all other conditions being identical and the foodstuffs having the same nitrogen and caloric value.

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**The Influence of Thirst on Nitrogen and Chlorid Metabolism.**

*Käte Frankenthal, Ztschr. f. klin. Med., 92:208, Berlin, Nov. 15, 1921.*

An 8 kg. dog served as the experimental animal. The diet consisted of 40 gm. dried horse meat, 30 gm. rice cooked in 60 c.c. water, and 40 gm. cod-liver oil, containing 5.66 gm. nitrogen and 0.29 gm. sodium chlorid, with 60 c.c. water. Such a rigid deprivation of water was borne only four days; on the fifth the animal was

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in great distress. On the first thirst day, there was marked retention with a small urine volume. The concentration of urine increased from the second day on, yet nitrogen retention was present on the fourth day. On the fifth day 6.86 grams nitrogen were retained; an increased nitrogen destruction in thirst was not shown. The sodium chlorid elimination is independent of the mass of fluid introduced, but adjusts itself to the diet. In the presence of scanty Na Cl ingestion, with limited water intake, and likewise during the period of thirst, the body eliminates more salt than is ingested, while with an abundant chlorid intake, a tendency to retention occurs. If a large amount of water is retained, sodium chlorid is always retained with it. The elimination of nitrogen is not disturbed by a small store of water in the body. The assimilation of food during thirst likewise does not suffer. With repetition of the experiment (4 times) an adaptation of the organism arises. There occurs damage in the sense that absorption in the intestine decreases; the assimilation powers become less; the fluctuations in the metabolic balance grow smaller; nitrogen retention constantly decreases.

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**Amino-Acids in Nutrition. IV. A Modified Biologic Method of Studying Amino-Acid Deficiencies in Proteins. Cystin as a Growth-Limiting Factor in the Proteins of the Georgia Velvet Bean (*Stizo-Lobium Deerigianum*).**

*Barnett Sure, J. Biol. Chem., 50:103, Jan., 1922.*

Cystin is unquestionably a growth-limiting factor in the proteins of the Georgia velvet bean. The experimental data preceding this conclusion are tabulated in graphic form. Chart 1 indicates that when Georgia velvet beans are fed as the only source of protein at a level of 40%, very little growth takes place, and that arachin, one of the globulins and the main protein from the peanut, does not furnish amino-acids to supplement those deficient in the velvet beans. At a definite point 0.4% of the ration was added in the form of cystin, but no response was obtained. Chart 2 shows that, in the presence of gliadin, there is a definite response to cystin addition to the velvet bean proteins, which is not, however, very marked two weeks after this amino-acid addition. Chart 3 indicates that zein appears to supplement the proteins of the Georgia velvet bean in the earlier periods of growth, but after eight weeks the nature of the growth is considerably retarded. The addition of cystin at a definite point brought about a slow improvement in growth with no further increase in the character of growth on the addition of tryptophan to the cystin at this point. This experiment, together with the one recorded in Chart 2, strongly suggests that cystin is a growth-limiting factor in the proteins of the Georgia velvet bean, which becomes apparent only after other amino-acids are satisfied, as supplied by such deficient proteins as gliadin and zein. Chart 4 indicates that gelatin does not furnish the necessary missing links deficient in the proteins of the velvet bean. Chart 5 is a duplicate of Chart 4, the experiment being repeated with heavier animals. After the addition of 0.4% of the

ration in the form of cystin, all the animals, although they had previously failed to make any growth and produced only maintenance curves on the same ration in this experiment, began to grow in a very marked manner for a period of ten weeks after the amino-acid addition, after which time the experiment was discontinued. This experiment furnishes conclusive evidence that, providing other amino-acids in the form of the deficient protein (gelatin) are supplied, cystin shows itself up well as one of the determining growth-limiting factors in the proteins of the Georgia velvet bean.

The remaining charts indicate that a slow but definite response to cystin was secured in the gliadin-velvet bean and the zein-velvet bean rations, but no response followed the addition of prolin even in the presence of cystin and tryptophan. The author concludes that cystin is a determining growth-limiting factor in the proteins of the Georgia velvet bean, a fact which becomes apparent only in the presence of such definitely deficient proteins as gliadin or zein, and most markedly in the presence of gelatin.

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**After-Effects of Trivial Influences on Metabolism in the Following Days.**

*W. Arnoldi, Ztschr. f. klin. Med., 92:187, Berlin, Nov. 15, 1921.*

Arnoldi studied, by means of the Zunst-Geppert apparatus, the after-effects on the blood sugar of subcutaneous adrenalin injections or grape sugar injections on the days following. The sugar content of the serum varied physiologically between 0.06 and 0.12%, biologic processes influencing the figures, such as the introduction of blood, glycogen storage, and influences on the sugar immobilisation. It was found that 1 administration of 100 gm. whey malt exercised a striking influence on the blood sugar for several days. The gas exchange for the two following days was considerably altered. The after-effect of the injection of 1 c.c. suprarenin continued for six days. For the first two days the blood sugar did not change, on the third and fourth days it was doubled. Gas exchange again showed definite changes. After a carbon dioxid bath there was on the next day a fall in blood sugar, followed by a sharp rise. On the whole the effects of grape sugar and suprarenin are similar: reactions were set up by both substances, which appeared on the following day and later. After ingestion of carbohydrates, examination of the gas exchange showed diminution of the oxygen and carbon dioxid, but an increase in the respiratory quotient. After suprarenin, increase of oxygen and carbon dioxid occurred with a rise of the respiratory quotient. Cases of endogenous obesity and hyperglycemia were typically different from the normal cases. The carbohydrate turnover was so increased in endogenous obesity that the carbohydrates were burned more slowly and the blood sugar remained normal. In hyperglycemia the carbohydrate consumption did not increase to bring the blood sugar to normal. The rise of blood sugar after suprarenin and grape sugar was small (glycosuria was absent). After several days the consumption of sugar was enormously increased, so that normal blood sugar values again were present.

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**Organic Foods with Specific Effects.**

*Emil Abderhalden and Ernst Wertheimer, Pfüger's Arch. f. d. ges. Physiol., 191:258, 279, 192:163, 174, Oct. 24, Nov. 12, 1921.*

In further researches on the action of accessory foods (vitamins, nutramins) it was shown that substances can be isolated from yeast and bran which strongly accelerate yeast fermentation. Nutramins also promote the increase of yeast cells. They increase the exchange of gases in whole animals as well as in isolated cells and, conversely, their deficiency (avitaminosis, beri-beri) is attended by diminished gaseous exchange. Further, they are supposed to have an influence on the activity of glands and on intestinal peristalsis. As their chemical characterization is not possible, various substances were examined for their action on red blood-corpuscles, on hepatic, renal, pulmonary and muscular cells and on frog's skin, by experiments on cellular respiration (oxygen consumed). Among the amino-acids, glutamic acid, pyrrolidin carbonic acid and glutamin increased respiration distinctly. The action was least on brain substance, which was distinctly influenced by tryptophan though the latter is inactive on muscle. With the exception of the brain, all tissues showed increased respiration upon the addition of rape-oil and particularly of cod-liver oil, which is probably due to as yet unknown substances. Milk increases respiration only slightly but does not lose its action entirely even by boiling for half an hour. Sour whey acts more strongly. Lactic acid is also effective, as are fatty acids but not their sodium salts, so that hydrogen-ion is obviously essential. Oxyacids act less strongly and ketone acids and their sodium salts (pyroracemic acids) very strongly. Aldehyd and crotonic acid were inactive, sodium fructose diphosphate slightly active, glyceryl phosphoric acid strongly active, and lecithin inactive. Primary potassium phosphate acts strongly, the secondary salt weakly and the tertiary not at all. Caffein increases oxygen consumption of muscle substance but not that of blood-corpuscles, heart substance or brain substance. Sodium arsenate acts only on muscle and skin. Antiscorbutic plant extracts are active. If the respective substances are coctostable both the antiscorbutic and the respiration promoting action is preserved after boiling. Only extracts of yeast and bran affect the oxygen consumption of white and gray nerve substance. It was shown, supplementarily, that light does not influence the respiration of unsensitized blood-corpuscles. Eosin increases the consumption of oxygen by diffused light, whereas direct sunlight has a distinct retarding action. The sun at high altitudes has the same effect.

If guinea-pigs be fed for some time exclusively on maize, barley, oats, peas, they contract typical scurvy, which may be treated with the antiscorbutics employed in human beings. The question arises whether these facts differ completely from the symptoms that are observed in pigeons fed exclusively on polished rice. Under such conditions body temperatures and gas exchange are reduced in pigeons. Guinea-pigs showed no characteristic behavior of body temperature, and respiration remained the same, on the whole, and could not be influenced by antiscorbutics (lemon juice, orange juice, dandelion). Spasms, which appeared concurrently with the intestinal hemorrhages,

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were also not influenced, whereas yeast autolysate, or alcoholic yeast extract, gave excellent results. Affections resembling scurvy are observable in pigeons. In both animal species the symptoms show far-reaching similarity. The same applies to pigs. Further experiments, which are related to the question of the influence of single nutramins on definite kinds of cells, were undertaken to determine the possibility of increasing or stimulating growth of hair by definite products. Experiments with aptinethylester hydrochlorid, peptone from feathers, as well as extracts from hair and from guinea-pig skin, gave negative results. No promotion of hairgrowth was ever observed. Whether the thickness of the hair can be influenced has not been determined.

In starving pigeons, the body weight decreases severely, and the exchange of gases sinks to values which are seldom reached in animals affected with alimentary dystrophy in consequence of feeding polished rice exclusively; the animals remain fresh, and the body temperature sinks only slightly. Animals fed on rice exhibit a slower decrease of weight, a gradually sinking and frequently irregular exchange of gases, and a decrease of the body temperature. The addition of yeast sometimes produces a slight increase of the exchange of gases and of the temperature in the starving animals and a distinct increase in those fed on rice. The pigeons affected with alimentary dystrophy show a decrease in the number of red blood-corpuscles down to 50% of the normal figure, the hemoglobin either being proportionally reduced in quantity or showing somewhat higher values than would correspond to the number of blood-corpuscles. Yeast produces an increase of appetite. Starving animals which had received yeast towards the end of the period taken up by the experiment greedily fell upon the food after its termination, whereas the others approached it with some hesitation. The decrease of the body temperature in alimentary dystrophy precedes certain other phenomena, especially spasms. The latter can always be relieved afresh by yeast preparations.

Muscular substance of pigeons fed on polished rice exclusively, and thereby affected with alimentary dystrophy, shows diminished respiration, which is extraordinarily increased upon the addition of yeast. The tissue respiration is considerably decreased even when there is only a slight decrease of weight as yet, in the case of muscle as well as brain and liver cells. Addition of yeast always increases the tissue respiration, so that the values of oxygen are higher than in normal animals. The latter also show the influence of yeast preparations by increased respiration, even though the increase in the consumption of oxygen is not so considerable. The alimentary dystrophy of pigeons is therefore distinguished by a decrease of the cell respiration and consequently of the whole gaseous metabolism. At the same time, there is a decrease of the body temperature; possibly, the spasms of such animals are connected with decreased respiration of the nervous system. The nutramins are perhaps necessary for the preservation of a certain condition of the cell content, or they may exert an influence on the limiting layer of cells and thereby on the metabolism. There is an analogous decrease in the exchange of gases to be observed in organs of guinea-pigs suffering from scurvy and also affected with spasms.

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The Occurrence of Urea in Nature. Theory of the Mode of Formation of Urea in Plants and in Animals. Cyanic Acid in Its Relation to Protein Degradation.

Emil A. Werner, *Dublin J. M. Sc.*, 4:577, Jan., 1922.

It is likely that each of the chemical changes in the body could be initiated in vitro if the full mechanism of each change were known. Werner proved (1912-1920) that in all syntheses of free urea, the final change is direct union of ammonia and cyanic acid in the keto form, O-C-NH. Is there any reason to suppose that free urea is produced otherwise in the living cell? The favorite theory of the origin of urea, however, has been the dehydration of ammonia or carbamate and the production of cyanic acid as the immediate precursor of urea was not contemplated. As a matter of fact, cyanic acid must be found in the liver; otherwise, urea would not be found there. The presence of urea is, in Werner's opinion, the most convincing evidence that cyanic acid was its precursor. He concludes that the formation of natural and of artificial urea in the free state is similar in mechanism. Most of the chemical changes taking place in plants and in animals are effected through the agency of the enzymes. In every instance in which an enzyme (or the preparations containing the active elements called enzyme) responsible for any definite chemical change has been isolated from its natural source, it has been found to reproduce the particular change in vitro under conditions not different, as to temperature, pressure and nature of solvent, and on the same lines as when in the living organism. The reciprocal action of animal and plant life in relation to carbonic acid and carbon assimilation is well recognized. From carbon dioxid and water, plants build up complex carbohydrates from which animals derive energy in oxidizing them to the 2 simple substances from which they were formed. Similarly, plants absorb ammonia, which is oxidized in the presence of carbohydrates to cyanic acid, which is used in the building up of protein matter. Animals, by hydrolytic and oxidation changes, break down proteins to cyanic acid and ammonia, which are excreted as urea, from which plants again derive the necessary material to continue the cycle of changes. The chemical analogy between the simple compounds concerned in the 2 changes of interest: O=C=O and H-O-H in carbohydrate formation, HN=C=O and H-(NT)-H in protein formation, the similarity between the oxygen atom and the amino group (NH) being recognized in many cases among carbon compounds.

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On the Synthesis of Uric Acid in the Human Organism.

Gustav Kollmann, *Biochem. Ztschr.*, 123:235, Berlin, Nov. 5, 1921.

In the course of an investigation on the prolonged nutrition of human beings on a diet poor in purin, it was found that from 0.5 to 1.0 gm. were eliminated per day, although the amount ingested could not have exceeded 0.3 to 0.5 gm. This made the synthetic formation of uric acid in the human organism conceivable, and various other observations seemed to point to the possibility of such a synthesis in

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adult human beings. If it could be shown that the amount of purin bodies eliminated during a lengthy experimental period materially exceeds the amount ingested, without loss of body-weight, the assumption of uric acid synthesis would receive support. Accordingly, experiments were carried out on a girl, aged 26, whose initial weight was 56.2 kg. The diet was practically free from purin and was continued for seven weeks, during which the daily elimination of uric acid was recorded. The dietary consisted of 5 eggs, 70 gm. butter, 600 c.c. milk, 300 gm. soft crackers, 150 gm. apple sauce, 300 gm. groats with milk and 350 gm. white bread. Green vegetables, coffee, cocoa and soup were omitted entirely. The food was examined for purin, not more than 0.1 gm. being detected. The uric acid estimation was effected by Benedict and Hitchcock's colorimetric method. At the end of the experiment the girl's weight had increased by 3.9 kg. The average daily elimination of uric acid amounted to 0.42 gm. Hence, a daily excess of about 0.3 gm. under a daily supply of 0.1 gm. purin is obtained, which corresponds to 15 gm. excess purin eliminated in the course of the fifty days' experimental period. This experiment, therefore, supports the assumption of the synthetic formation of uric acid in the organism.

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**The Reactions of Inactive Malic Acid in Dogs and Rabbits.**

*M. Tomita, Biochem. Ztschr., 123:231, Berlin, Oct. 25, 1921.*

Malic acid, like other vegetable acids, is partly oxidized within the organism, and partly excreted without undergoing any change. The writer desired to find out whether malic acid belonged to the group of compounds which can be asymmetrically decomposed. The results of the investigation corroborated this assumption. The experiments were undertaken upon dogs and rabbits, and the required inactive malic acid was obtained from maleic acid. The determination of malic acid was made by mixing 10 gm. of the sugar-free urea with acetic acid previously saturated with uranium acetate. The roughly filtered solution can be used immediately for purposes of optical determinations. This urea, which under direct polarization hardly rotates at all, under the influence of the uranium salt showed considerable rotation. The specific rotations of uranium-malic acid and glucose are in the ratio of 51.5:52.6. Therefore, it is only necessary to divide the indicated values by 0.78, in order to obtain in grams the amount of malic acid contained in the mixture.

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**The Conservation of the Functions of Aërobic Cells in the Replacement of Free Oxygen by Chemically Combined "Pseudo-Anoxybiose." III. Experiments on Spermatozoa.**

*Werner Lipschitz and Günther Hertwig, Pflüger's Arch. f. d. ges. Physiol., 191:51, Berlin, Oct. 24, 1921.*

Suspensions of frogs' spermatozoa, preferably in saline faucet water (which is more suitable than distilled water owing to its calcium content), are killed by treatment for two or three hours with pure oxygen, which is even more effective than hydrocyanic acid. The cells irreversibly lose their motility and, in contradistinction to muscle cells,

their capacity for reducing dinitrobenzol. In anaërobiosis (hydrogen atmosphere) the spermatozoa become motionless, but regain their motility upon the addition of easily reducible nitrogroups that take up oxygen. Hydrocyanic acid arrests movement even in weak concentration, though it does not inhibit vital processes entirely, as the reducing capacity persists even with higher concentration. As in the case of the oxid reducing cell processes so, here, a difference in the action of the stereo-isomeric fumaric and maleic acids takes place, the latter arresting movement while the former has no effect. But their action on the surviving frog's heart is practically identical.

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The Reduction of the Aromatic Nitro-Group as an Indicator of Partial Processes of Respiration and Fermentation. A Method for the Comparative Quantitative Estimation of Biologic Oxid Reductions.

*Werner Lipschitz and Alfred Gottschalk, Pflüger's Arch. f. d. ges. Physiol., 191:1, 33, Berlin, Oct. 24, 1921.*

*Experiments on Respiring Cells.*—The poisonous action of aromatic nitro-compounds (formation of methemoglobin and cell toxicity) depends on the reduction to b-phenylhydroxylamins. The processes at play in this reduction may correspond to cell respiration. Like it, they may suffer narcosis and are sensitive to hydrocyanic acid, so that the reduction from m-dinitrobenzol to m-nitrophenylhydroxylamin might be utilized as an indicator for cell respiration, in which, besides oxygen consumption and carbon dioxid formation, the migration of hydrogen plays a prominent part. The poison employed permits of a colorimetric method of studying this process. Experiments on respiring frog muscle cells showed that the reduction is dependent on a coferment, and that its curve corresponds, in time, with the respiratory curve. At 80° C. it is completely abolished and is confined to the intactness of the cellular structure. Increasing supply of oxygen retards reduction while with optimal oxygen concentration it is abolished (reversible). The influence of narcotics resembles that on respiration. The different agents give nearly linear curves for arrestment of reduction and of respiration. Combinations show additive effects. The law of homologous series holds in both cases. The arrestment curve of hydrocyanic acid is diphasic, in contradistinction to the respiratory arrestment curve, as it shows a minimum at 0.5% and 5% respectively. If the muscle be extracted with water the reducing capacity is lost, but it may be restored with muscle fluid, or yeast fluid, as also by such substances as succinic acid, citric acid, fumaric acid. Other substances, as maleic acid, dextrose, glycerin, are inactive. In conformity with this, unextracted muscles increase the reduction of succinic and fumaric acids while that of maleic acid and saponin is arrested.

*Experiments on Fermenting Cells.*—The problem to be investigated was the behavior of anoxybiotic cells toward the nitro reduction effect (also without consumption of oxygen and with production of carbon dioxid). Even strictly anaërobic cells, such as the cells of the united skin and muscles in *Ascaris megalcephala*, or *Bacillus butyricus*, strongly reduce the aromatic nitro group. Therefore, there exists a resemblance to a partial process of respiration and fermenta-  
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tion in the form of an intermolecular hydrogen migration in addition to the resemblances to carbon dioxide formation and the probable identity of the coferment in respiration and fermentation. The reduction is thermolabile, associated with the coferment, may be arrested by narcotics but not by supply of oxygen, and is not confined to intact cell structure but only to the presence of filterable cell débris. The behavior of the cells of the united skin and muscles in earth-worms is different, because reduction is here confined to the intact cell structure (the same in rape-seed embryos). The inhibition by hydrocyanic acid is incomplete in both cases, as also in *B. proteus* and *B. butyricus*.

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**Anesthesia.**

*Hermann Lange and B. W. Müller, Klin. Wochenschr., 1:23, Berlin, Jan. 1, 1922.*

The marked excretion of phosphoric acid by the muscle to the surrounding and external tissues, and the reverse, corresponds to increased permeability. This induced the authors to determine whether there was a relation between anesthesia and an increase or decrease of the permeability of the limiting cell membranes. Permeability was increased in long anesthesia and was again diminished after the anesthesia was stopped. There is a diminution in the permeability at the very beginning of narcosis. The transitory increase of excitability is demonstrable upon the use of concentrations of an anesthetic which are less than the concentration required for anesthesia. The real cause for anesthesia appears to be the diminution of the power of alteration of the limiting membrane, whose sudden increase of permeability leads to stimulation.

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**The Relations of the Static Current to Irritability.**

*Hermann Voelkel, Pflüger's Arch. f. d. ges. Physiol., 191:200, Berlin, Oct. 24, 1921.*

A relationship between cell polarization and irritability being assumed at the present day, relations between the latter and the static current would seem possible. For the alteration of irritability, narcotic poisons were employed (ether, chloroform). The static currents were determined with the Edelmann thread galvanometer on the customary nerve-muscle preparations exposed to the action of these substances. Static current and irritability were found to be wholly independent of each other, as the former was not influenced. It did not change during an increase of irritability at the commencement of narcosis and the difference in potential between longitudinal and cross section induced by the narcosis retrograde more rapidly (with oxygen supply) than the reestablishment of irritability advances. The symptoms were observed on the nerve as well as on the muscle. The narcosis, therefore, acts in the sense of a negation of the attacking point, to which the influence of the narcotics on the electric phenomena must be ascribed. Presumably one is dealing with an alteration of the internal distribution in the tissue portions that are exposed to narcosis.

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**The Study of the Action Current.**

*F. Kraus and S. G. Zondek, Deutsch. med. Wochenschr., 47:1513, Berlin, Dec. 15, 1921.*

The authors attempted to study the bio-electric forces in relation to the frog's heart, on isolated specimens of muscle. They attempted to determine the bio-electrical forces which occur in membranes separated by aqueous solutions. Absorption from the solution and mobility of the fluids which influence the forces of the membranous chain are to be considered.

Certain ions stimulate the frog's heart (Straub) OH and Ca are antagonistic to H, K, and Na. The electrolyte combination, as is seen in Ringer's solution, is the best medium in which to observe the Straub heart continue to beat with normal frequency and rhythm. The highest degree of water absorption, which may be observed even with the naked eye, is revealed by the preparation when water is employed. The effect of the water is seen electrographically by the very steep J (R), and especially the deep J p (S) serration. These are present to the very last.

The authors believe that the initial serrations are of the same significance in the clinically observed human cases, and that the deviations from the normal of these early groups of serrations are of the same nature. This is of importance in the practical diagnosis of the cardiac function. The effects of electrolysis on the tension affect the membranes. The electrolytes are adsorbed in certain places (electro static and mechanical adsorption, independent of each other). Membranes with variably specific adsorption will favor the concentration of certain solid substances. One substance crowds another away from the surface during the adsorption of several electrolytes. Changes in the surface tension, as well as adsorption, appear on the membranes.

There is a close connection between the permeability or impermeability of the surface and the adsorption. Contraction of the Ca heart, and relaxation of the K heart, indicates that the adsorption of the Ca heart is greater, and that it produces a more marked impermeability of the limiting surface (membrane); this is in proportion to the concentration of the limiting surface. The surface tension determines the shape, at least the temporary shape (length of the muscle) in the body of the animal. The tone probably depends upon some such simple process.

The action and tonus currents are to be explained by a capillary electric activity.

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**Physicochemical Investigations of the Nervous System. I. Turgescence and Double Refraction of the Medullary Sheath.**

*E. A. Spiegel, Pflüger's Arch. f. d. ges. Physiol., 192:225, Berlin, Nov. 12, 1921.*

Experiments on nerve-muscle preparations from frogs have shown that the double refraction of the excitable and the dead nerve is the same. It is based on forces exerting pressure in a radiate direction, which are closely related to the surface tension conditioned by mole-

cular attraction. The double refraction of the medullary sheath is modifiable by chemical processes affecting the glycerophosphatids, or by physical transformations modifying the forces exerting pressure in a radiate direction with respect to the longitudinal axis. As a matter of fact, a decrease of anisotropy is observed in consequence of turgescence, which may, in the end, lead to an inversion of the double refraction. Soaking is an easily reversible process, and on its cessation, the former optic conditions are restored. These facts may become significant with respect to Reichardt's theory of cerebral tumefaction. In order to investigate the influence of acidification on such processes, the nerves were treated with solutions of hydrochloric acid of a gradually increased concentration. Although a zone was found in which the acid caused a slight furtherance of the turgefaction, the vitality of the nerve was already destroyed in that case. In higher concentrations this furtherance decreases again, and in living animals this effect could not be produced either by the application of acid or by endogenous acidification (uranium nitrate poisoning) within the limits compatible with the life of the animals.

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**Physicochemical Investigations of the Nervous System. II.  
The Influence of Narcotics on the Anisotropy of the Nerve Medullary Sheath.**

*E. A. Spiegel, Pflüger's Arch. f. d. ges. Physiol., 192:240, Berlin,  
Nov. 12, 1921.*

The nervus ischiaticus of rats freshly killed by exsanguination was pulled to pieces and part immersed in physiologic solution of common salt and part in narcotics. After that, it was subjected to an examination for double refraction. The lipoid-solvent narcotics and similar substances, such as chloral hydrate decrease the double refraction of the medullary sheath and finally abolish it. Magnesium sulphate and cocaine, as well as high degrees of cold, did not influence the anisotropy in any way. The abolition of double refraction may be reversed by immersion in glycerin or by evaporation of the narcotic. Apparently the normal forces of radiate pressure are decreased by a comparatively loose combination of the narcotic and the myelin. From observations of the optic behavior combined with simultaneous stimulation experiments on the nerve-muscle preparation, it appears that the double refraction commences to decrease when the excitability is just beginning to be lowered, and that, on the cessation of the narcosis, anisotropy and excitability are restored at practically the same time.

Physicochemical considerations lead Spiegel to the conclusion that the observed effects must be attributed to decreased surface tension in the medullary sheath, and to the solution of the narcotics in the axon and the modification of the distribution of ions in the axoplasm resulting therefrom. Referring to Nernst, he attributes an excitatory effect to the modification of the distribution of ions, and thus accounts for the genesis of the stage of excitation during narcosis.

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Experiments to Determine the Nature of the Effects of the Vagus and Sympathetic Systems.

S. G. Zondek, *Deutsch. med. Wchnschr.*, 47:1520, Berlin, Dec. 15, 1921.

The vagus retards the heart, the sympathetic stimulates it. The reverse is true of the stomach and intestine. The author compares the effect of the inorganic cations on the functions of the organs discussed, in order to determine the nature of this action. The effects of sodium and potassium always resembled those of the vagus. The effect of calcium always corresponded to that of the sympathetic, in principle. Muscarin stimulates the bowel, adrenalin relaxes it (effect on the sympathetic), potassium stimulates while calcium relaxes the bowel. The nature of the effect appears to be the same. The various substances may be exchanged for one another. Calcium compensates the effect of muscarin, and adrenalin reverses the effect of potassium. The esophagus, stomach and bladder react in the same way. The effect on the uterus is interesting. Stimulation of the vagus causes contraction of the uterus. Stimulation of the sympathetic causes relaxation in most, but not in all cases. The latter depends upon the nature of the animal and upon whether or not the animal is pregnant. Adrenalin relaxes the uterus of the nonpregnant animal and contracts the uterus of the pregnant animal. Calcium has the same effect.

The author thinks that the potassium does not stimulate the vagus but that the vagus influences the potassium. The sympathetic influences calcium in the same way. Both nerves direct their corresponding ions to the point at which they are needed to aid the physiologic effects, as for example to cause contractions.

Nernst explains muscular stimulation by the electric current on purely physical grounds, by assuming that there is a necessary change in the concentration of the natural electrolytes in the border between the cell membrane and the watery solution. The author explains the mechanism of every nervous stimulation or excitation in the same way. This applies to the vagus and sympathetic nerves as well. The vagus and sympathetic divide the work of bringing about the difference of concentration of the electrolytes. The effect of the vagus is that sodium and potassium receive the greater part while the sympathetic influences the calcium to a greater degree. The nature of functional organic disturbances due to abnormal irritability of the vagus or sympathetic is to be sought in a disturbance of the physiologic combination of electrolytes.

The favorable effect of calcium in vagotonia has already been found empirically. Calcium which is the antagonist of the effect of sodium and potassium, should be given to counteract the effect of the 2 latter, or the intake of sodium and potassium should be reduced. The combination of both methods would be best. The reverse is probably true in cases of disease of the sympathetic system.

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**The Clasping Reflex After Extirpation of the Sympathetic.  
Tonic Innervation.**

*E. A. Spiegel and E. Sternschein, Pflüger's Arch. f. d. ges. Physiol., 192:115, Berlin, Oct. 29, 1921.*

In 12 frogs, the fourth sympathetic ganglion was severed unilaterally from its connection with the fourth spinal nerve, and the third ganglion from that with the third spinal nerve as well as with the second ganglion. The result of the operation was controlled by the histologic examination of the extirpated ganglia and the temporary stasis in the vessels of the web. No difference in the contraction could be established between the intact side and that which was operated upon either by lifting the heavier female in the state embracing or by inserting a wedge between the two animals. Author concludes that the sympathetic is not involved in the genesis of the tonic innervation of the skeletal muscles.

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**The Doctrine of the Muscular Tonus. II. Condition and Innervation of the Muscles of the Anterior Extremities of the Frog During the State of Embracing.**

*R. H. Kahn, Pflüger's Arch. f. d. ges. Physiol., 192:91, Berlin, Oct. 29, 1921.*

Experiments undertaken under appropriate conditions, by diverting the action currents of the muscles of the anterior extremities of the frog, show that the latter are devoid of current during the tonic permanent contraction, whereas voluntary contractions or reflex contractions, in consequence of traction, are accompanied by action currents in the manner of tetanic muscular spasm. In the present case there is, just as in the closure of bivalvule shells, a tonic permanent contraction without any discoverable bio-electric symptoms. The innervation of the muscles in question is effected by the brachial plexus, i. e., tie ventral branches of the second, third and fourth spinal nerves, which also contain efferent fibers from the second, third and fourth sympathetic ganglia. In order to decide the question, as to whether these tracts play a part in effecting the permanent contraction, experimental poisoning was resorted to.

The general paralysis effected by curare includes the loosening of the muscles which are contracted during the state of embracing, but their complete paralysis ensues somewhat later than that of the other muscles. This alone shows how improbable it is that sympathetic innervation is involved. Adrenalin apparently produces a lowering of the muscular tonus; but the particular muscles concerned here are less affected than any others or not at all. Physostigmin increases the reflex excitability, but does not lead to a permanent contraction. Pilocarpin loosens the embrace without any additional phenomena. Atropin does not exert any influence even in large doses (10 mg. and more in a solution of 1%). The separation of the third and fourth sympathetic ganglia from the spinal nerves, the severing of the ansa just below the subclavian and of the fasciculus marginalis below the fourth spinal nerve make it possible to disconnect all sympathetic fibers leading to the muscles by which the embracing is ef-

fected, but the latter is not loosened thereby. It may therefore be considered as certain that this typical permanent contraction of a transversely striated muscle of a vertebrate is not conditioned by sympathetic innervation.

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**Transformations of Energy in Muscle: Lactic Acid Formation and Mechanical Work. V.**

*Otto Meyerhof, Pflüger's Arch. f. d. ges. Physiol., 191:128, Berlin, Oct. 24, 1921.*

If the frog's gastrocnemius muscle be allowed to work up to the point of exhaustion by irritation with single induction discharges, oxygen being excluded (hydrogen atmosphere or Ringer solution), its maximal lactic acid content reaches 0.35%, but rises to about 0.5% if the Ringer solution be rendered alkaline with carbonate-bicarbonate, under which the performance of anaërobic work increases materially, while the amount of lactic acid (in milligrams) per tensional capacity (in kilograms) for each centimeter of muscle diminishes slightly (isometric coefficient). The muscle's fatigue maximum is induced by the lactic acid concentration in the interior of the muscle, as is shown by the distribution of lactic acid between the muscle and the surrounding liquid. The isometric coefficient falls in the course of anaërobic fatigue. It is smaller by one-third during the second half of fatigue than during the first half, but is independent of the amount of contraction. Under the influence of narcotics it falls still further, also under potassium chlorid though not as strongly. It must be assumed that narcotics displace lactic acid from the contracting surfaces. As the coefficient falls with increasing duration when the muscle is irritated by brief tetany, though not in proportion to the number of effective stimuli, the stimuli required to maintain the tension produce less lactic acid than the stimuli serving for the development of tension. The calculations hitherto employed for determining the capacity for mechanical work of the energy released by irritation, are subjected to thorough theoretic and experimental criticism. If one compares the new values for the effective work performed, and for the formation of lactic acid, one obtains the work coefficient for lactic acid and, hence, the anaërobic efficiency of the muscle, if 100 calories are assumed for the formation of 1 mg. lactic acid. Direct determination gives lower values than indirect determination. With higher temperatures the degree of efficiency is lower than with lower temperatures. The oxidative efficiency has a value of 20-24%. A higher oxidative efficiency than one of 30% is not known and would correspond to an anaërobic one of 60%. Probably the maximum potential energy developed by irritation never exceeds 75% of the total energy. In that case the thermochemical energy demanded by the splitting up of glycogen to form lactic acid, to which about one-quarter of the entire heat of contraction is due, would not have to be utilized. Experiments on gastrocnemii in guinea-pigs give the same results as those in frogs. The chemical and mechanical processes in mammalian muscle do not appear to be related to each other any differently from those in the muscle of cold-blooded animals.

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**Changes in Muscular Strength During Movement.**

*J. H. O. Rejs, Pflüger's Arch. f. d. ges. Physiol., 191:234, Berlin, Oct. 24, 1921.*

The researches extended to palmar and dorsal flexion of the hand, pronation, supination, stretching and bending the elbow-joint, abduction and adduction of the shoulder-joint, dorsal and plantar flexion of the foot, abduction and adduction of the leg, bending the body backwards, and finally the strength of hand pressure and the lifting power of the muscles of the back. The curves all show a fairly simple form, the greatest strength being obtained at the point at which the muscles perform most work. This point is noted on the curve and supplies the basis for the design of therapeutic gymnastic apparatus (resistance) as also for the construction of tools and for prostheses. Experiments on 2000 individuals showed that left-handed persons are not as numerous as those possessing greater strength on the left side of the body. The relative strength of men and women measured dynamometrically, is in the proportion of 5:3. Change in strength with increasing age shows a steeper ascent in men and reaches its maximum at 24 years, in women at about 22. In women decline is somewhat more rapid.

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**The Galvanic Irritability of Human Skeletal Muscle After Intravenous Injection of Highly Concentrated Calcium Solutions.**

*Martin Nothmann, Arch. f. exper. Path. u. Pharmakol., 91:312, Leipzig, Nov. 4, 1921.*

The direct galvanic irritability of human skeletal muscle is increased by physostigmin. Conversely to the action of oxalated blood, which increases irritability, the author now tried that of afenil, then 25 c.c. of a 10% calcium chlorid solution, intravenously, for their action on the galvanic irritability of the ulnar nerve with Stintzing's normal electrode of 3 sq. cm. The reduction of electric irritability is lowest in cathodal closure contraction, more marked in anodal closure contraction, very pronounced in cathodal closure tetanus and strongest with anodal opening contraction. In tetany and guanidin toxications, the alteration of electric irritability is observed in the opening contractions. The phenomena is strongest fifteen to twenty minutes after the injection.

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**The Formation of Inorganic Phosphoric Acids in Contraction of the Muscles of the Frog.**

*Gustav Embden and Hans Lawaczeck, Klin. Wchnschr., 1:23, Berlin, Jan. 1, 1922.*

The formation of free phosphoric as well as lactic acid in muscular contraction was demonstrated only in the white muscle of rabbits and dogs. The demonstration was unsuccessful in the frog up to the present because the building up of the lactacidogen balanced the splitting off of phosphoric acid. The authors succeeded in demonstrating the phosphoric acid by submerging the muscle, at the beginning of the contraction, in liquid air until it

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was frozen. Phosphoric acid is split off at the beginning of the contraction, but is used in the formation of lactacidogen, even while the muscle is still in a state of tetanus.

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**The Relation of Muscular Rigidity and the Relations Between Intumescence and Coagulation of Muscle Albumin.**

*Hans H. Weber, Pflüger's Arch. f. d. ges. Physiol., 191:186, Berlin, Oct. 24, 1921.*

Whereas muscular rigidity unquestionably depends on lactic acid swelling, the cause of its relaxation is still a matter of controversy. It may be considered to arise from an accumulation of lactic acid and subsequent swelling, or from disappearance of the acid. Experiments with collodion membranes impenetrable to albumin but penetrable to water and salts, showed that detumescence cannot account for the relaxation of rigidity, because with elimination of albumin loss muscular intumescence constantly increases. Coagulation, whether spontaneous or produced by heat, does not bring about detumescence. At times, detumescence is increased by the concurrently developed lactic acid, even if the albumin has already coagulated. Coagulation takes place only with neutral particles whose active participation in the combination of water in the muscle is not measurable. The amount of these particles (electrolytic discharged albumin-ions) determines the reception of coagulation. The assumption that a relationship exists between coagulation and detumescence (Fürth) is based on an erroneous interpretation of the loss of weight in muscles, which latter arises not from loss of water, but from loss of substance due to the withdrawal of liquefied albumin. The origin of this loss of substance from excessive swelling may be determined by direct measurement. Consequently, the view that the relaxation of rigor mortis depends on excessive swelling of the contractile structure induced by lactic acid receives support.

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**The Creatin Content of Frog's Muscle in Hypnotic Rigidity.**  
*Herbert Schönfeld, Pflüger's Arch. f. d. ges. Physiol., 191:211, Berlin, Oct. 24, 1921.*

Reflex tonus and active permanent contraction of the muscle are related to the formation or exclusion of creatin, whereas true static tonus does not increase, and may even diminish, creatin formation in muscle. If frogs be put in a state of immobility in the dorsal position, rigidity of the posterior, or more often of the anterior, extremities is produced, which is presumably due to centrally induced increase of reflex tonus. Frogs kept in a state of rigidity in this way for three hours were decapitated during anesthesia, the adductors of the posterior extremities being then immediately prepared for the creatin examination. The values obtained with these muscles in various animals agreed well. The estimation was effected colorimetrically (Dubosq apparatus). In all experiments the average increase of creatin amounted to 21.49%.

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**The Physiology of Respiration.**

*Leon Asher, Schweiz. med. IVchnschr., 52:1, Basel, Jan. 5, 1922.*

Respiration is not an isolated function but a regulating measure for fundamental conditions of life. Breathing as an interchange of gases is only one of the manifestations of metabolism. The starting point of respiration is the "internal breathing," the process of  $\text{CO}_2$  formation and using up of oxygen in the cells of the body. The discovery of the carboxylases (Neuberg), enzymes which free carbonic acid by a splitting of the carboxyl group, as, for instance, from amino-acids, is a new and important contribution to the non-oxidative origin of carbonic acid. Siegfried's carbanin acid reaction also reveals new ways in which nonoxidative  $\text{CO}_2$  may arise. Carbonic acid also appears in the absence of oxygen, as in the muscles. This is not newly formed, but comes from preformed carbonates and acids. Respiration does not proceed to the end-stage—carbonic acid—but stops with the higher organic acids.

The relation between internal respiration and fermentation is shown by a study of the conditions of life without oxygen, or with very much decreased oxygen. There is a co-ferment of breathing which corresponds to the co-ferment of fermentation. Both are influenced to the same degree by narcotics. Neuberg succeeded in understanding the intermediate steps in the breaking down of sugar, pyroracemic acid and acetaldehyd, substances which are met with in internal respiration. Neuberg's discovery of sugar-free fermentation is also important for the proper comprehension of internal breathing. This concerns substances which arise not only from sugar but also from albumin and fat, at least in the animal body.

Oxidative respiration is always of the first importance. The need of energy causes the oxidative breaking-down of albumin, fat, and carbohydrates. This oxidative breaking down is accompanied by the formation of acids and other organic acids, as well as  $\text{CO}_2$ . The oxidative processes are the real sources of energy, and this is why there is such a need for oxygen.

The extent of internal respiration is judged by a determination of the oxygen and carbonic acid content of the arterial and venous blood of the several organs. This is how the interchange of gases was determined in the salivary glands, kidneys, pancreas, muscles and heart, in both the active and the resting stages. The consumption of energy may be determined from the consumption of oxygen. The air in the alveoli is that part of the pulmonary air which is concerned in the interchange with the blood. The expiratory blood consists of the portion from the "injurious area" and from the alveoli. Only the latter can give information as to the processes going on between the blood and the pulmonary air. The most important finding of Haldane and Priestley was that the carbonic acid tension in the alveolar air always remains the same under physiologic conditions, and that every change of the  $\text{CO}_2$  tension changes the respiratory ventilation uniformly. This is the basis for their teaching that the  $\text{CO}_2$  tension of the blood circulating through the respiratory center regulates the respiration. All of

the foregoing concerns the chemically hematogenous regulation of the breathing.

The functions of the breathing center may also be regulated by centrogenous and peripheral stimuli. There is only a single medullary respiratory center, and not a secondary one in the spinal cord. Diminished CO<sub>2</sub> tension of the alveolar air does not necessarily mean acidosis or diminution of the alkali reserve, at any rate not in the beginning. However, it may have this effect. It may also be due to increased sensibility of the respiratory center, which requires a lower level of oxygen ion concentration. Such increased sensibility may be due to the action of pharmacologic substances, during the stage of excitement which they may produce, or it may be due to the effect of short exposures to artificial sunlight, or to several other influences. Above all, diminished CO<sub>2</sub> tension may also be due to a primary centrogenous stimulus of the respiratory center. Henderson has emphasized the practical importance of this point.

The CO<sub>2</sub> of the blood is lost to an abnormal degree as a result of protracted ether narcosis or excessive ventilation of the lungs. Henderson called this poverty of CO<sub>2</sub> "acapnea," and shows that the carbonate alkalis are removed secondarily—not a result of acidosis—and in a regulatory manner. A diminished CO<sub>2</sub> tension of the alveolar air is observed, which is not due to acidosis. The disagreeable results of an unsuitable ether narcosis in trauma and operations on the viscera are avoided by inspiration of air containing 6-7% of CO<sub>2</sub>. This is shown by the fact that there is no diminution of the CO<sub>2</sub> capacity of the blood, exclusive, marked drop in the blood pressure, or other signs of shock. The inhalation of CO<sub>2</sub> in genuine acidosis is dangerous. There is a marked disturbance of the cardiac diastole in complete absence of CO<sub>2</sub>. A high degree of diminution of oxygen also produces hyperpnea when the CO<sub>2</sub> already formed is lost. This hyperpnea has a different subjective and objective character than CO<sub>2</sub> dyspnea. This leads to the assumption that there is hyperpnea of centrogenous origin in lack of oxygen and superventilation of CO<sub>2</sub>. This leads to alkalosis, and this in turn to a regulatory diminution of the alkaline carbonates.

Carbonic acid tension which is above normal may indicate increased alkali capacity—the opposite of acidosis—or diminished sensibility of the respiratory center. Morphin manifests its inhibitory influence on the respiratory center by the increased alveolar CO<sub>2</sub> tension, which is easily demonstrable. The relation of respiration and the circulation is of importance.

Fick says that the consumption of O<sub>2</sub> in 100 c.c. of blood is to the total consumption per minute as 100 is to the quantity of the minute volume. Krogh employs the nitrogen oxid method for the determination of the minute volume of the heart. The lost quantity of the indifferent gas is found by determining the air which is contained in the lungs and the percentage difference of the nitrogen oxid content determined by analytic methods. Two more physiological facts are worthy of notice. One is that every determination of the minute volume may be inconclusive due partly to the influ-

ence of psychic elements or to excitement of the vasomotors, with its consequent effect on the circulation. This applies to the determinations at rest. The test runs smoothly in the determinations during work. The other factor is the one observed by Loewy and consists of respiration failure on the part of certain subjects during muscular exertion, which is not, however, due to increased carbonic acid or to diminished oxygen tension of the blood. Loewy concludes that this dyspnea is due to other products which are formed during muscular exertion.

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**The Physiology of Glands. Relations Between Thymus Gland, Spleen and Bone-Marrow.**

*Leon Ascher, Cengo Matsuno, Biochem. Ztschr., 123:27, Berlin, Oct. 25, 1921.*

The spleen does not seem to have a uniform function. Injections of thymus gland extract postpone muscle fatigue. Absence of the thymus gland increases considerably the function of the thyroid gland. The writer tried to establish experimentally the relation between the thymus gland and bone marrow by examining the blood. By means of the relative white blood pictures he determined the amount of hemoglobin before and after removal of the thymus gland.

To make the results more pronounced 2 operations were performed, venesection and experimental anemia by a chemical poison, prussic acid. As venesection and the lack of oxygen have an irritating effect upon the bone marrow, applying these 2 operations before and after removal of the thymus gland, determines at the same time the faculty of bone marrow to react to a measurable irritation under 2 different conditions.

In the case of some animals (rabbits were used) not only the thymus gland but also the spleen was removed. Hemoglobin was determined by Sahli's method. The red and white blood-corpuscles were cultivated in Thomas' apparatus. The histologic blood picture was examined by the methods of May-Gruenwald and Romanowsky-Giemsa. The blood was taken from the ear vein. The results show that after the removal of the thymus gland the amount of hemoglobin is diminished, but normal conditions are soon re-established. The number of lymphocytes increases, while the number of leukocytes diminishes. But the results are much more pronounced when the 2 irritants of the bone marrow are used, namely, venesection and injection of a small quantity of prussic acid. In the case of normal animals the number of lymphocytes drops considerably and the number of leukocytes increases even more, immediately after venesection and the introduction of prussic acid. After removal of the thymus gland venesection and prussic acid cause only a very slight diminution of the amount of hemoglobin and the proportion between leukocytes and lymphocytes is hardly influenced at all. The removal of the spleen has little effect upon the symptomatic picture of a missing thyroid gland. Absence of the thymus gland diminishes the reactive power of bone marrow. This leads to the conclusion that the thymus gland has a favorable

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influence upon the bone marrow, and that its presence is of much greater importance, provided it is in good functional condition, than that of the spleen.

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### The Nature of Innervation and Its Relation to Internal Secretion.

*Emil Abderhalden, Klin. Wchnschr., 1:7, Berlin, Jan. 1, 1922.*

The recent perception of innervation is that it is not a direct influence on the organ supplied, but that it is an indirect phenomenon brought about by products formed under the influence of the excited nerve. The following points are gleaned from the literature: Fluids which flow through a heart which is under the influence of a stimulated vagus become richer in potassium. Increased secretion of the salivary glands and stomach is brought about by substances formed under the influence of the nerves of secretion. Stimulation of the vagus or of the sympathetic nerves to the heart would appear to cause the formation of a "parasympathetic substance" and a "sympathetic substance," respectively. These substances are caused by stimulation of the nerves and affect either the cardiac centers or the muscle itself (Loewi). Transfer of blood serum from the hearts of warmed animals and the reverse influences the sugar metabolism. It seems that substances are formed, under the influence of warming and chilling, which circulate in the blood and increase or decrease cell oxidation. Seemingly, also, the path to the central warmth regulating center passes through the thyroid. Injection of thyroid extract and other substances in hibernating animals (hedgehogs) leads to increase of temperature, and in waking animals to increase of the cellular oxidation. The experiments of Krogh, Abderhalden and Gellhorn show the influence of endocrine substances on the musculature of the small vessels and indicate an associated effect of nervous influences and specifically acting products. Recent experiments show the influence of the sugar center on the adrenals by way of the sympathetic nerves; a substance, which is formed as a result of this, has to do with the breaking down of glycogen by the liver-cells. All these observations show an intimate connection between the effect of endocrine substances and nervous influences.

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### The Relations between Cholesterin and Suprarenal Capsules in the Rabbit.

*Carlo Alessandri, Riv. crit. di clin. med., 22:397, 409, Florence, Dec. 5, 15, 1921.*

Experiments with adrenalin were made by the author on healthy rabbits and on rabbits from which one or both suprarenal capsules had been removed, to determine the effect on the cholesterin content of the blood. Subcutaneous and endoperitoneal injections caused a slight increase of cholesterin which varied with the amount of adrenalin and with the time elapsing between the injection and measurement. The minimum injection was 1.4 c.c. per kilogram of weight, and the minimum time was two hours.

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Subcutaneous injection caused a greater increase in a rabbit that had lost one capsule than in a normal one, and this evidence increased in proportion to the number of days elapsing after the operation. In cases of removal of both capsules the increase of cholesterinemia was slightly less. It was found to bear a certain relation, but not a very marked one, to the amount of glucose found in the urine for the twenty-four hours after the injection. The results are shown in a series of 5 tables.

It has been demonstrated that the injection of adrenalin causes an increase of cholesterinemia in the organism. Three hypotheses are possible to explain this fact: (1) the suprarenal capsules alone are stimulated, either forced to secrete more cholesterol or to mobilize cholesterol already there; (2) the capsules are not affected, but all the tissues of the organism are forced to its mobilization; (3) the capsules and the other tissues are stimulated together. It is evident that in those rabbits from which both capsules had been removed the increase of cholesterol could not come from capsules that were lacking, but must come from other organs or tissues. In other words, the capsules are not indispensable to the cycle of cholesterinemia. The reaction of the whole organism must then be admitted. The most striking effect of adrenalin in the organism when introduced artificially is in the vasomotor centers, especially the vasoconstrictor. It is this vasomotor action, rather than the direct action of adrenalin upon the parenchymal cells, that causes the mobilization. The latter would then be a mechanism of defence on the part of the organism, because to cholesterol is attributed a marked antitoxic function; this mechanism would be more intense or lasting according to the necessities of the organism or of some of its organs. Among these would be included the suprarenals, because they are richer in cholesterol and undeniably closely related to it; but even they must be liable to the same consequences of artificial introduction into the blood of adrenalin (adrenalinemia).

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**Results of Hyperthyrmization.**

Rudolf Demel, *Mitteil. a. d. Grenzgeb. d. Med. u. Chir.*, 34:437, no. 4, Jena, 1922.

With the view of studying the effect of hyperthyrmization on the osseous system and the glands of internal secretion the author implanted in rats 3 weeks old, from the same litter, pieces of thymus tissue from rats of the same age, from rats 2 months old and rats 8 months old. The implantations were made in a muscle pocket between the buttock and thigh. Later examination showed that the implants took well, that the tissue was well preserved and that therefore it was justifiable to assume that function was preserved. The implants had no effect on the animal's own thymus gland. The animals were livelier and stronger than the control animals, had more fat and more rapid growth. The thymus of young animals was much more effective than that of sexually mature animals, but the thymus did not become totally inactive after sexual maturity. The bones of the hyperthyrmized animals

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were slenderer than those of the control animals, but were not less strong. The epiphysis was higher than in control animals, and consisted of regularly arranged columns of cartilage cells. The vesicle-shaped cells on the side toward the metaphysis were larger and paler than those toward the epiphysis. Some of them projected quite a distance toward the marrow space of the metaphysis, so that the boundary line was broken in places. The bone trabeculas of the metaphysis of hyperthyroidized animals was different from that of the control animals. The latter formed a looser network and the trabeculas were fewer in number and quite uniformly distributed, while in the former they formed a close network with fine, pronouncedly longitudinal meshes. The experiments did not show any functional effect of hyperthyroidization on the adrenals, the sexual glands or the hypophysis. The feeding of thymus substance (0.5 gm. daily in the form of Pochl's thymus tablets for two months to rats 4 weeks old) did not show any effect on the skeleton or endocrine glands.

#### 1b. BIOLOGIC AND ORGANIC CHEMISTRY

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##### The Preparation of Flexible Collodion Membranes.

*Joseph M. Looney, J. Biol. Chem., 50:1, Jan., 1922.*

Method for obtaining extremely flexible collodion membranes. The procedure is as follows: Five grams of "Anthony's Negative Cotton" which has been dried for forty-eight hours over concentrated sulphuric acid, are placed in a clean and dry Erlenmeyer flask, 25 c.c. absolute ethyl alcohol are added, and the flask is agitated so that all the cotton is thoroughly moistened. Then 75 c.c. ether, which has been distilled from sodium, are added and the flask is shaken until the cotton has completely dissolved. Then 15 c.c. of ethyl acetate are added with shaking to secure complete mixing of the solvents. The solution is allowed to stand over night and then the clear supernatant liquid is decanted off into another flask. The membranes are prepared inside of test-tubes or Kjeldahl flasks and may be made of any desired size. The solution is poured into the flask, which must be perfectly clean and dry, and the excess of collodion is allowed to drain back into the container by holding the flask at an angle of about 60° and slowly rotating it until the collodion no longer drips freely and then the flask is clamped upside down in a stand and left until it is completely dry. When the membrane is perfectly dry it is removed by peeling the top of the film from the neck of the flask and then pouring a gentle stream of water between the membrane and the side of the flask, which frees the membrane so that it can be withdrawn. The appearance of pin-holes in the membranes may be avoided by using only scrupulously clean and dry flasks.

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##### Direct and Indirect Determinations of Permeability.

*W. J. V. Osterhout, J. Gen. Physiol., 4:275, Jan. 20, 1922.*

Osterhout believes the most satisfactory method of determining the penetration of substances into the living cell is to place the cell  
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in a solution containing the substance whose penetration is to be investigated and, after a definite time of exposure, to obtain the cell sap without contamination and test it for the presence of this substance. The author performed such experiments, using the large multinucleate cells of a species of Nitella. The cells are placed for the desired length of time in a solution containing the substance whose penetration is to be tested. They are removed, washed in running tap water and dried by means of filter paper. The cells are so large and turgid that this manipulation is not difficult. A cell is then placed on a piece of glass or filter paper and pierced with the point of a clean capillary tube. The cell sap is drawn up into the tube (by capillary action) quite free from protoplasm or chloroplasts. Tests of the cell sap obtained from Nitella without contamination showed that in a balanced solution of  $\text{NaNO}_3$ , plus  $\text{Ca}(\text{NO}_3)_2$  there was a slow penetration of  $\text{NO}_3$  and the cell remained in a normal condition, but in pure  $\text{NaNO}_3$  there was rapid penetration accompanied by injury.

The author had previously determined the permeability by the indirect methods of plasmolysis and electrical conductivity so he compared the results with those obtained by direct tests of the cell sap. The observations on recovery from plasmolysis gave similar results, though the method is less satisfactory. The determinations of electrical conductivity gave the same result, so it may be concluded that this method gives reliable information regarding permeability.

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**The Penetration of Cations into Living Cells.**

*Matilda Moldenhauer Brooks, J. Gen. Physiol., 4:347, Jan. 20, 1922.*

By employing a large form of Nitella the author was able to investigate the penetration of several cations from balanced and unbalanced solutions. This species of Nitella was selected because of the length of the multinuclear cells and the amount of cell sap which may be expressed from a single cell. The cells were placed in approximately neutral hypotonic solutions of the cations Li, Cs, and Sr. Direct tests of the cell sap showed that the protoplasm is normally permeable to Li, Cs, and Sr, and that penetration is more rapid in an unbalanced than in a balanced solution.

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**A Simple Presentation of the General Properties of Colloids.**  
*W. M. Bayliss, Lancet, 202:38, London, Jan. 7, 1922.*

The colloidal state is recognized, in that the particles of the material in such solutions are of dimensions too large to pass through the pores of certain membranes, and yet small enough to remain in permanent suspension. They are so maintained by Brownian movement (the result of the molecular movement of the water molecules) and electric charge. Various colloids differ much in their sensibility to electrolytes, the metallic ones being very sensitive and unstable. One colloid can also discharge and precipitate another, if they possess electric charges of opposite signs. The addition of a trace of gelatin makes colloidal metal far less sensitive to foreign salts, due to the ad-

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sorption of a layer of gelatin by the surfaces of the particles. Gelatin and other emulsoids are not nearly so sensitive as the metallic colloids. Many other compounds, such as the various products of hydrolysis of proteins, are also effective; commercial preparations of colloids, with the exception of those made by the electric method, contain protectives of some kind. Many of these protectives have themselves a powerful physiologic action, so that unless it is known what is present and what its effect is, any therapeutic effects noticed can be claimed to be due to the metallic colloid itself. The absence of a protective colloid is therefore an advantage. Those preparations made by the electric method instead of by a chemical one would be preferable, except that they are apt to settle out on standing, on account of the difficulty of excluding all foreign electrolytes. When these preparations are used intravenously or intramuscularly, the proteins of the blood and tissues act at once as protectives against the salts also present, and there is no need for an artificial protective. If sodium chlorid or any other salt is added to the preparation in order to make it isotonic with blood, it is necessary to have a protective for the colloid. The small doses used, however, present no risk; a nonelectrolyte, such as sugar, would be as effective as a salt and would require no further protection. Such a protective as the arabinic acid of gum acacia is not in organic combination with the colloid, but is merely adsorbed. An important distinction must be made between suspensoids and emulsoids. The dispersed phase in the former is in the form of solid particles, such as gold, sulphur, ferric hydroxid, free from water. They are more sensitive to electrolytes and therefore less stable than the latter class, which includes gelatin, albumin and other proteins, and silica. Here the dispersed phase contains more or less water, absorbed (imbibed) into the solid particles. The amount of water or degree of swelling can be altered by the presence of salts or other electrolytes. But it should be remembered, in view of such theories of edema as those of Martin Fischer, that a fairly high strength of acid is necessary to produce any notable effect. Emulsoids are far less sensitive to this ionic influence than are suspensoids. Up to the present no good evidence has been produced to prove that the chemical or pharmacologic action of substances in the colloid state differs from that in true solution, otherwise than in the matter of gradual slow effect. The striking characteristic of the colloid state is the existence of an enormous extent of surface. One of the properties dependent on this is the electric charge. If an electropositive colloid, such as ferric hydroxid (ordinary colloidal iron), is injected into the blood, which contains electronegative colloids, mutual precipitation will occur with serious results. But no satisfactory evidence has yet been produced to prove that the electric charge as such has any physiologic action. The fact that colloids do not diffuse through the walls of the blood-vessels renders possible the use of certain colloidal dyes, in the estimation of the volume of the blood. Another property of physiologic importance is the osmotic pressure exercised by certain emulsoid colloids, gelatin, gum arabic, and the proteins of the blood. It is this property which prevents the rapid loss of fluid from the blood by filtration through the capillary walls and controls the production of

urine. Added to saline solutions, gum arabic prevents their loss from the blood, which otherwise takes place very quickly after intravenous injection.

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**The Origin of the Electric Charges of Colloidal Particles and of Living Tissues.**

*Jacques Loeb, J. Gen. Physiol., 4:351, Jan. 20, 1922.*

When a solution of a salt of gelatin or crystalline egg albumin is separated by a collodion membrane from a watery solution (free from protein) a potential difference is set up across the membrane in which the protein is positively charged in the case of protein-acid salts and in which the protein is negatively charged in the case of metal proteinates. The turning point is the isoelectric point of the protein. Measurements of the pH of the (inside) protein solution and of the outside watery solution show that when equilibrium is established the value pH inside minus pH outside is positive in the case of protein-acid salts and negative in the case of metal proteinates. At the isoelectric point where the electric charge is zero, the value of pH inside minus pH outside becomes zero also. The author shows that a potential difference is established between suspended particles of powdered gelatin and the surrounding watery solution and that the sign of charge of the particles is positive when they contain gelatin-acid salts, while it is negative when the powdered particles contain metal gelatinate. At the isoelectric point the charge is zero. Measurements of the pH inside the powdered particles and of the pH in the outside watery solution show that when equilibrium is established the value pH inside minus pH outside is positive when the powdered particles contain a gelatin-acid salt, while the value pH inside minus pH outside is negative when the powdered particles contain Na gelatinate. At the isoelectric point the value pH inside minus pH outside is zero. The addition of neutral salts depresses the electric charge of the powdered particles of protein-acid salts. The addition of salts to a suspension of powdered particles of gelatin chlorid also diminishes the value of pH inside minus pH outside. In the author's experiments the agreement between the values 58 (pH inside minus pH outside) and the potential difference observed by the Compton electrometer is not only qualitative but quantitative. This proves that the difference in the concentration of acid (or alkali, as the case may be) in the two phases is the only cause for the observed potent difference. The Donnan theory demands that the potential difference of a gelatin chlorid solution should be 1½ times as great as that of a gelatin sulphate solution of the same pH and the same concentration (1%) of originally isoelectric gelatin. This was found to be correct in the author's experiments, it was also shown that the values of pH inside minus pH outside for the 2 solutions possessed the ratio of 3:2. All these measurements prove that the electric charges of suspended particles of protein are determined exclusively by the Donnan equilibrium.

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The Correlations between Blood Plasma and Tissue Fluids, Particularly between Aqueous Humor and Cerebrospinal Fluid.

I. Sugar Content and Combined Sugar.

*J. de Haan and S. von Crefeld, Biochem. Ztschr., 123:191, Berlin, Oct. 25, 1921.*

The relation between blood and lymph, and the reciprocal action between blood and tissue fluids is still a matter of discussion. Blood pressure is not the only effective filtration force for the formation of lymph, but the work of cells plays a certain part. Consequently, if any chemical differences are encountered between the tissue and blood driving forces, they must be governed by two factors. Either they are the expression of an extremely strong modifying work of the tissues, or else the impermeability of the membrane for certain bodies is almost complete. But even in the latter case a very slight difference in the production and consumption of these bodies on both sides of the membrane would cause a great difference in concentration. This explains the variation in albumin content of blood and lymph. The present investigations are based upon this chemical point of view, and were undertaken in order to establish the relation between the blood and 2 typical organic fluids—the aqueous humor of the anterior chamber of the eye and the cerebrospinal fluid, both of which can easily be obtained in a pure state. For the determination of permeability glucose, a physiologic product, was used. It was also determined to what extent the sugar content of these tissue fluids under normal conditions differed from that of the blood, and for this artificial variation, at short intervals, of the sugar content of the blood was produced. The speed with which the tissue fluids reacted to these variations served as a measure of permeability of the membranes to glucose. Both of the fluids are noted for their low content in albumin and other colloids. It was known previously that the red blood-corpuscles of the circulating blood are entirely sugar-free, but that the slightest alteration, like defibrination or coagulation, caused a quick transfusion of the greatest part of the plasma sugar into the blood-corpuscles. In every case in which whole blood or blood plasma was examined the sugar content was lower than in circulating plasma.

The blood sugar contents of an animal is exposed to considerable fluctuations. No definite values could be obtained and it was necessary to make the determinations in the blood and in the other fluids, as far as possible, at the same time. All of the sugar in the plasma seems to be present in a free state, but experiments indicate the probable existence of combined sugar. As aqueous humor and cerebrospinal fluid possess almost all the properties of an ultrafiltrate, a study was made to determine whether these fluids acted like an ultrafiltrate of the blood so far as their sugar content is concerned, or if, on the other hand, the existence of combined sugar within the circulating plasma could be proved. The material was taken from a rabbit and the sugar content was determined by Bang's method, while the albumin content was determined refractometrically. Hypoglycemia was produced by subconjunctival injection of a 1% adrenalin solution. For ultrafiltration one of Waard's small filters was used. The results of these investigations indicate that the glucose content of tissue fluids that are

practically free from colloids (aqueous humor, cerebrospinal fluid), is lower than of blood-plasma. Consequently, part of the blood sugar must be combined, and these fluids react like an ultrafiltrate, or dialysate of the blood. As in an ultrafiltrate, the combined sugar remains behind in vitro. The blood-corpuses of venous, as well as of arterial blood, are sugar-free, and a simultaneous examination of the ultrafiltrate shows that the lower sugar content of the venous plasma relates only to the free sugar. This indicates that the free sugar is being used up constantly. The results of adrenalin hyperglycemia indicate that within these fluids the speed of diffusion of plasma sugar is quite high, and the corresponding value is approximately the same for both fluids. At first, diffusion proceeds somewhat more slowly than under normal conditions, on account of the effects of adrenalin upon the vascular system. The average sugar content of normal aqueous humor differs considerably from that of the blood plasma. Secondary aqueous humor, which is regenerated very quickly, contains the greatest part of the plasma colloids, as well as the combined sugar. Its sugar content corresponds to that of the plasma at the same moment. The average sugar content of the cerebrospinal fluid remains far behind the corresponding values for plasma and aqueous humor. The difference in the sugar content of cerebral plasma and aqueous humor is due to the fact that there is a greater consumption of cerebral sugar. This is an expression of the organic work of the brain. The sugar content of the posterior facial vein is lower than that of the carotid artery blood collected at the same time. This difference is caused by free sugar, which indicates that the latter is being used up in the tissues. The increased sugar content of plasma after an injection of adrenalin is also due to free sugar.

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**Do the Lymphocytes Contain a Lipolytic Ferment? Lipase Content of the Cerebrospinal Fluid.**

*Alfred Resch, Ztschr. f. klin. Med., 92:160, Berlin, Nov. 15, 1921.*

Beregl attributed the lipase of exudates to the lymphocytes present in such exudations, believing that the lipase arises from the lymphocytes. Resch studied this problem in relation to cerebrospinal fluid in various diseases, and found not the slightest relation between lymphocytosis and lipase in a quantitative way. The methods of Michaelis and Rona were employed in estimating the lipase. A tibutyrin solution was mixed with the fluid and examined by the stalagmometric method. An optional ionic concentration must be maintained; for the purpose were added 0.1 c.c. N/3 primary sodium phosphate plus 2.0 c.c. N/3 secondary sodium phosphate, thus maintaining a hydrogen-ion concentration of  $1.0 \times 10^{-8}$ . Control experiments with heated spinal fluid yielded only a very slight splitting of the tibutyrin solution into butyric acid and glycerin, and so very little change in the drop-count. There could be shown no constant relationship in purulent meningitides or chronic diseases even with a very high lymphocytosis in the spinal fluid, in contrast to the lipase content determined by this method. Especially significant is Caro's finding that in a case of lymphatic anemia, which showed a 39—56 fold increase

of lymphocytes in the blood, no rise of the lipase in the serum could be demonstrated. Lymphocytosis can be a factor constitutionally limited.

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**The Relation of Some Cyclic Compounds in Human and Animal Organisms.**

*Erich Schempp, Hoppe-Seyler's Ztschr. f. physiol. Chem., 117:41, Berlin, Nov. 10, 1921.*

Phenyl acetic acid in dogs, rabbits and monkeys combines with glycocol to form phenaceturic acid, and in birds it unites with ornithin, whereas in man it combines with glutamin to form phenylacetyl glutamin, in which form it is excreted. An explanation for these differences in the intermediate metabolism in various animals was sought. The urine was collected for twenty-four hours after the last intake, made alkaline with  $\text{Na}_2\text{CO}_3$ , evaporated to a syrupy consistency, acidified with phosphoric acid, and extracted with a solvent.

Phenylacetic acid was fed to cats and chickens. In the former phenyacturic acid (melting point  $143^\circ$ ), and in the latter, phenacetornithuric acid were found. The nitrogen determination yielded identical values, whereas the melting point was higher, and in contrast to Totani, gave no dextrorotation in alcoholic solution. Ingested orthonitrophenylacetic acid could be recovered in dogs as well as in men. This was also the case for paranitrophenylacetic acid. Phenylbromacetic acid appears as inactive amygdalic acid in which the splitting of the HBr occurs spontaneously upon the addition of the Na salt. After the ingestion of thiophenic acid, thiophenuric acid (melting point  $177^\circ$ ) was excreted. After ingestion of pyromucic acid there was excreted pyromucic acid, pyrincuric acid (melting point  $165^\circ$ ), furfuracrylic acid (glycocol combination), and pyroncurate of urea.

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**A Biochemical Explanation of the Silica Molecule.**

*P. R. Vessie, Med. Rec., 101:106, Jan. 21, 1922.*

Silica is widely scattered in essential food products. While found by analysis in all structures and organs of the body, it is notably present in the connective tissue cells. Laboratory methods demonstrate that bacteria have the ability chemically to reduce soluble silica. It follows that bacteria may digest the silica molecule as well as other components of the human cell. Since silica is the preponderant neutral salt in the connective tissue cell, bacteria may dissipate it, causing a famine of this element at the site of bombardment. If the human economy has a sufficient supply of silica in reserve, temporary silica starvation at the point of bacterial attack is immediately remedied by a replacement of silica molecules. When nature fails to act with such favorable promptness, certain types of pyogenic bacteria (staphylococci) may gain a foothold at a focal point within in the body. In the event of suppuration, a defensive barrier of connective tissue, loaded with silica molecules, is formed around the nucleus of pus organisms to resist their systemic advance. The pyogenic bacteria then become less potent from want, or even perish by self-destruction

when successfully pocketed by a silica zone. This theory is applicable to a person with tuberculosis who faces a condition of silica hunger, "silication" is impossible, because the bacteria continue to feast on the systemic supply of silica. If silica is reduced as nearly as possible to an atomic state, e. g., in a colloidal form, it may serve as a remedy. Sodium silicate is such a compound. It is of a colloidal nature and assimilable to form colloidal salicic acid (a true colloid). In this form it enters the circulation and combines with bases to yield a highly complex derivative which, when it is distributed, affects other molecules in greater or less degree. A change in the character of the connective-tissue cell is thereby produced; by giving the cell the proper impulse with its own specific substance (silica), the inhibited molecules reset themselves to a normal grouping and speed.

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**Sodium Persulphate in the Analysis of Phosphorus Compounds.**

*L. Débourdeaux, Bull. d. sc. pharmacol., 29:20, Paris, Jan., 1922.*

Phosphorus may be determined in triargentic phosphate by using sodium persulphate to transform the phosphorus to phosphoric acid, and to eliminate carbon from organic compounds. Phosphites and hypophosphites may be oxidized by the persulphate. Determinations are shown for  $\text{Na H}_2\text{PO}_2$ ,  $\text{K}_2\text{HPO}_3$ , and  $\text{Na}_2\text{HPO}_2$ . The process is described for organic compounds, Ag acting as catalyst. It is rapid and easy, precautions required by alkaline combustion are obviated, and organic matter is eliminated. Each gram of the sample analyzed is dissolved in 100 to 150 c.c. water. A few cubic centimeters of  $\text{HNO}_3$ , at 40° Baumé, are added, then the sodium persulphate required for combustion, and finally the  $\text{AgNO}_3$  required to precipitate phosphoric acid. Carbon is burned off as usual. When the brown color indicating complete combustion appears, the liquid is boiled for an hour or two on the water-bath to get rid of the excess of persulphate. Any precipitated silver sulphate is redissolved by ammonia, and triargentic phosphate is precipitated by careful neutralization with  $\text{HNO}_3$ . The method corresponds to that for determining arsenic in arsenical compounds. The quantity of P, Cl and Ag in organic compounds may be determined by eliminating carbonaceous matter with sodium persulphate. The determination of lime and magnesium in compounds is indicated. (*To be continued*)

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**Copper Salts of the Aminosulphonic Acids.**

*R. Demars, Bull. d. sc. pharmacol., 29:14, Paris, Jan., 1922.*

In organic compounds formed from ammoniocupric salts, the ammonium is linked to the central Cu atom. Such a compound, copper glycocolate, for example, may behave either as an acid or a base. Nickel compounds resemble those of copper. The action as acid or amin (base) is important in the production of blue copper compounds. In a carbon chain, SO may take the place of C,  $\text{SO}_2$  may represent CO, etc. Possibly Cu may have a similar analogy, in compounds with  $\text{SO}_2\text{OH}$ , to its compounds with carboxyl. The question is whether both sets of compounds consist of closed chains having the same num-

ber of links. Three carboxyl and sulphonic compounds are compared. The blue color appears to be deeper in salts in which the amin function is separated from the sulphone function by an atom of C, as in the alpha-amino-acids. The point could be proved in only one of the copper compounds,  $[NH_2 \cdot CH(SO_3K)SO_3]_2 Cu$ . The results obtained with the phenyltaurins are indecisive.

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**The Chemistry of the Oxidation of Sulphur by Microorganisms to Sulphuric Acid and Transformation of Insoluble Phosphates Into Soluble Forms.**

*Selman A. Waksman and Jacob S. Joffe, J. Biol. Chem., 50:35, Jan., 1922.*

When sulphur is added to unsterile soil, it is slowly oxidized to sulphuric acid; when the soil is previously sterilized oxidation of the sulphur takes place only to a very limited extent, depending upon the other chemical substances present. But when a sulphur-oxidizing organism is introduced, the sulphur is rapidly oxidized to sulphuric acid. The authors isolated several organisms which were able to oxidize sulphur under various conditions. One such organism was an aërobic, autotrophic, minute bacterium, *Thiobacillus thiooxidans*, Waksman and Joffe, which was able to oxidize sulphur to such an extent as to reduce the hydrogen-ion concentration of the medium to a pH of less than 1.0 even in the presence of buffering materials. Its energy is derived from the oxidation of the sulphur and of the carbon from the carbon dioxide of the atmosphere. The nitrogen can be supplied in the form of inorganic or organic materials. The authors prepared mixtures of sulphur, rock phosphate and soil inoculated with crude cultures of sulphur-oxidizing organisms; one set was aërated and the other left unaërated. The amount of phosphates brought into solution and the change in the hydrogen-ion concentration, as expressed by the exponent pII of Sorensen, were used as criteria. The aërated mixtures were leading and after one hundred days, the percentage increase of soluble phosphates in the aërated over the non-aërated was 6%, with a similar correlation in the increase of the hydrogen-ion concentration.

In regard to the oxidation of sulphur in the ordinary cultivated soil, the authors report experiments to indicate the mechanism of sulphur oxidation in the soil, both in the absence and in the presence of small and large amounts of rock phosphate. The sulphur and phosphate were added to the soil and well mixed. A crude well developed culture was used for inoculation. The moisture content of the soil was kept at an optimum by the addition of water at weekly intervals. The cultures were incubated at 25-27° C. The pH values were determined colorimetrically according to the method of Clark and Lubs; the phosphates and sulphates according to the method of the Official Agricultural Chemists. It was learned that the transformation of insoluble rock phosphate to soluble phosphates by the sulphuric acid formed from the oxidation of sulphur by *Thiobacillus thiooxidans* is similar to the process taking place in inorganic reactions. The curve of sulphur oxidation, both in the soil and in solution, by pure and impure cultures

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of *Thiobacillus thiooxidans*, is a growth curve, the mechanism of sulphur oxidation to sulphuric acid by this organism obeys the laws of inorganic catalysis.

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**The Inactivation of Trypsin.**

*John H. Northrop, J. Gen. Physiol., 4:227, 245, 261, Jan. 20, 1922.*

Modern studies of individual enzymes have shown that few, if any, obey the law of mass action in its simplest form. It is known that various substances retard the action of enzymes which implies a reaction between these substances and the enzyme. If it could be shown that this reaction conformed accurately to the law of mass action it would furnish experimental justification for the application of this law to the enzyme reaction in general, at least as far as the particular enzyme is concerned. It has been shown by the author that the equilibrium between pepsin and the products formed by its action on proteins does conform quite accurately to the law of mass action. The experiments described in this paper were undertaken with the view of determining whether or not the same condition is found in the case of trypsin. It was found that the solution resulting from the hydrolysis of the protein by trypsin was strongly inhibitory and such solutions were, therefore, used although it was not found possible to determine exactly what chemical compound was responsible for their reaction. The inhibiting solution was prepared from salt-free gelatin brought to the isoelectric point. The trypsin used was a sample of Fairchild's trypsin, a solution of which was made fresh daily. For determination of the conductivity the apparatus used was a Leeds and Northrup Kohlrausch bridge and resistance box. A special type of conductivity cell (illustrated and described in the article) was used. In addition to showing experimentally that it is possible to prepare a solution by the action of trypsin on a protein which inhibits the action of trypsin, the author has demonstrated that the amount of this retardation can be quantitatively measured by comparing the time necessary to cause a given change in the conductivity of the gelatin solution under the conditions adhered to.

*Equilibrium between trypsin and inhibiting substance.*—This article attempts to account qualitatively for the retardation quantitatively measured in the preceding series of experiments. A study was made of the equilibrium existing between trypsin and the substances formed in the digestion of proteins which inhibit its action. This substance could not be obtained by the hydrolysis of the proteins by acid or alkali. It is dialyzable. The equilibrium was studied by varying (a) the concentration of the inhibiting substance, (b) concentration of trypsin, (c) concentration of gelatin, and (d) the concentration of trypsin and inhibitor (the relative concentration of the two remaining the same). In all cases the results agreed quantitatively with those predicted by the law of mass action. It was found that the percentage retarding effect of the inhibiting substance on the rate of hydrolysis is independent of the hydrogen-ion concentration between pH 6.3 and 10.0. Inactivated trypsin did not enter into the equilibrium.

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*Spontaneous Inactivation.*—In addition to the inactivation of trypsin caused by its combination with some of the products of hydrolysis and discussed in the first article of this series, the author states that trypsin undergoes a second or spontaneous inactivation which is independent of the action of the enzyme. This inactivation is also irreversible and distinct from the reversible retardation of the action of the enzyme by the products formed during the reaction. Previous workers who studied the inactivation of trypsin observed the reaction was not monomolecular but became progressively slower than the rate predicted by the monomolecular formula, from which it was concluded that the solution contained a number of different forms of the enzyme some of which were more stable than others. It was also noted that the purity of the solution had a marked influence on the rate of decomposition. In the experiments described in this paper the author employed the methods recorded in the preceding articles of the series. The amount of active trypsin present was determined by measuring the time required for 1 c.c. of the solution to cause a small amount of hydrolysis of a gelatin solution at 33° and a pH of 6.2. The hydrolysis was followed either by the formol titration or the change in conductivity. Then the influence of the containing vessels, the influence of the purity of the solution on the course of the reaction, the influence of the manner in which the inhibiting solution was added, the influence of the pH on the rate of decomposition, and the influence of the pH on the protective effect of the inhibiting substance, as individual factors were each separately observed. The author found that the rate of inactivation of purified trypsin solutions approximates closely that demanded by the monomolecular formula. The products formed by the action of trypsin on proteins renders the trypsin more stable. Gelatin and glycine were found to have no such effect. The rate of inactivation of trypsin solutions containing these products did not follow the course of a monomolecular reaction but became progressively slower than the predicted rate. The protective action of these substances was found to be much greater if they were added all at once at the beginning of the experiment, rather than at intervals. Northrop believes these observations may be quantitatively accounted for by the hypothesis that a compound is formed between trypsin and the inhibiting substance which is stable as well as inactive, and the rate of decomposition depends on the amount of uncombined trypsin present.

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**Xylans.**

E. Salkowski, *Hoppe-Seyler's Ztschr. f. physiol. Chem.*, 117:48, Berlin, Nov. 10, 1921.

The methods heretofore given for the production of xylan from straw is modified in that the alkaline solution of the straw is not treated with Fehling's solution immediately after filtration, but diluted to 7 liters and allowed to stand a few days. It is then filtered from the precipitate, evaporated to the original volume and filtered through asbestos. The precipitate is easily dissolved in

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NH<sub>3</sub> with heat, is then filtered and strongly acidified with HCl, diluted 1½ times with 95% alcohol, and let stand for precipitation of the xylan. The gelatinous precipitate is freed of water; the fat is removed with absolute alcohol and ether, and the salt is rubbed dry. The xylan thus obtained (a light cream colored powder which shows the characteristic reaction with orcin) is soluble in NaOH and in saturated Na<sub>2</sub>CO<sub>3</sub> solutions but not in glacial acetic acid. As a differentiation from yeast gum and gum arabic, it gives a heavy precipitation with basic lead acetate, with HCl and phosphotungstic acid and with tannin. The analysis of the elements showed the formula C<sub>5</sub>H<sub>8</sub>O<sub>4</sub> given by Tollens. This was supported by the fact that quantitative determination of xylose obtained by hydrolysis from a known quantity of xylan shows that the xylan takes up one molecule of water in hydrolysis. Computation of the xylose from the copper obtained by heating with Fehling's solution (reckoned from Cu<sub>2</sub>O) yielded values differing from Stone's, 0.51 for a 0.25% solution and 0.5527 for a 0.1% solution, but only when a pure aqueous solution is used. The reducing power diminishes upon heating with HCl as is the case with glucose. The results obtained by conversion of xylose into the phloroglucid approached those determined according to the Krober table.

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**The Solubility of Acetyl Cellulose in Salts of Alkalies and Alkaline Earths.**

*K. Schweiger, Hoppe-Seyler's Ztschr. f. physiol. Chem., 117:61, Berlin, Nov. 10, 1921.*

In the course of investigations upon cellulose in salts of alkalies and alkaline earths, studies were made upon the solubility of acetyl cellulose preparations of different German firms in strong solutions of LiCl, LiBr, LiI, LiNO<sub>3</sub>, NaCl, NaBr, NaI, CaCl<sub>2</sub>, CaBr<sub>2</sub>, CaI<sub>2</sub>, Ca(CNS)<sub>2</sub>, SrCl<sub>2</sub>, KHgI<sub>3</sub>, and ZnCl<sub>2</sub>. Acetyl cellulose (0.5—1.0 gm.) was digested in 10-15 c.c. of the salt solution at room temperature for two or three days, and at 100° C. for six hours with frequent shaking. At the end of the experimental period the solubility was tested by dilution with water. The studies with LiCl, BrNO<sub>3</sub>, NaCl, NaBr, CaCl<sub>2</sub>, and SrCl<sub>2</sub> gave negative results. The acetyl cellulose content of the solution could be increased up to 20-30% and more; for example, in Ca(CNS)<sub>2</sub>, on the whole, according to the tables, the same solubility relationship seemed to apply as with cellulose. It is noteworthy that at higher temperatures, solutions show considerably greater internal friction than at lower temperatures. The reduction figures indicate that the concentrated salt solutions do not attack the acetyl bond, but split the cellulose molecule. The stability of the esters can also be shown by experiments with octacetyl-celllobiose and pentacetylglucose. Both combinations, insoluble in water, are soluble in Ca(CNS)<sub>2</sub> without evidence of saponification. The same is true with nitrocellulose.

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**Dry Yeast.**

*B. von Euler and Karl Myrback, Hoppe-Seyler's Ztschr. f. physiol. Chem., 117:28, Berlin, Nov. 10, 1921.*

The fermentation produced by fresh yeast is almost stopped by substances such as toluol, chloroform, ether, whereas the free zymase as it occurs in a Buchner press juice is hardly influenced by the same anticeptics. Quantitative determinations of the peculiar enzyme components and of the activators of the zymase system were made, and the course of fermentation with unchanged dry yeast and pressed yeast was studied with different kinds of sugar, to determine the influence of drying and extraction through different solvents, and the influence of toluol and other protoplasmic poisons on the different fermentation phases. The yeast was dried; for a ferment substrate, cane sugar, maltose, invertase or glucose was used. The fermentation was carried out at 0.7% PO<sub>4</sub>, with an optimum acidity (pH-4.5), and at 30° C., and was studied volumetrically. The concentration relations in fermentation were studied first with changing amounts of yeast. It was found that there was a relation between the amount of yeast and the rapidity of fermentation. In studying the effect of changing amounts of ferment solution it was shown that the rapidity was doubled (expressed in cubic centimeters of CO<sub>2</sub> per hour) when yeast and sugar were halved. It was plainly shown that the quotient CO<sub>2</sub> hours increases with time, indicating that the yeast gradually becomes more active. Washing the dry yeast, especially the top yeast, with water even when long continued, and with or without previous treatment with alcohol, indicates that the extraction of activators was very insignificant. Also in the studies with bottom yeast no results from washing with water were obtained. On the other hand by washing with 2% Na<sub>3</sub> PO<sub>4</sub> the yeast became in time less active though even after prolonged washing a greater part of zymase remained. Finally it was determined how many grams of dry yeast were required to yield activators that would bring 8 gm. washed yeast to maximal fermentation. For this, the dry yeast was rubbed with 2% phosphate solution and then warmed over the water bath for one-half hour at 78°, by which the zymase was destroyed while the activators remained intact. Then the course of fermentation with different amounts of this dry yeast was followed. The maximum fermentation was obtained by the addition of activators from 8 gm. dry yeast to the zymase from 1 gm. of dry yeast.

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**Dismutation of Different Aldehyds by Yeast.**

*H. Kumagawa, Biochem. Ztschr., 123:225, Berlin, Oct. 25, 1921.*

Animal organs possess the property of transforming aldehyds according to the course of Cannizzaro's reaction. On account of the biochemical interest of the reaction of dismutation in the decomposition of animal and vegetable products of metabolism, the writer tried to determine the effect which yeast in solutions of bicarbonates had upon some other aldehyds. He investigated one

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aromatic and three aliphatic aldehyds (benzaldehyd, isobutylaldehyd, isovaleric aldehyd and oenanthol). It was found that these four aldehyds underwent dismutation in solutions of sodium bicarbonate in the presence of yeast. The dismutation of benzaldehyd is only very slight in solutions of sodium bicarbonate, but the addition of yeast increases it considerably. Theoretically, it was to be expected that two molecules of aldehyd would produce one molecule of the corresponding alcohol and one molecule of the corresponding acid. But on account of a considerable addition of yeast, the polysaccharids contained in it caused a phytochemical reduction, and some of the alcohol was also transformed into acid. The experiments were conducted in the following way: The aldehyd was added to a suspension of 500 gm. yeast in 1 liter of a 1% sodium bicarbonate solution and the mixture was well shaken. This was placed in an incubator at 35° C. until the odor of aldehyd had disappeared. Half of the mixture was then used for a determination of the alcohol produced, and the other half for the determination of the acid. Ten gm. isovaleric aldehyd yielded 1.72 gm. amyl alcohol and 3.5 gm. valeric acid; 10 gm. isobutyl aldehyd produced 0.86 gm. isobutyl alcohol and 1.04 gm. isobutyric acid; the same amount of oenanthol yielded 1.72 gm. of heptyl alcohol and 1.02 gm. of the corresponding acid; 10 gm. benzaldehyd gave 2.21 gm. benzyl alcohol and 1.01 gm. benzoic acid with a melting point of 118°.

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**Pyroracemic Acid as an Intermediate Product of Alcoholic Sugar Fermentation.**

*Max von Grab, Biochem. Ztschr., 123:69, Berlin, Oct. 25, 1921.*

Neuberg studied the fermentation of pyroracemic acid, and found that this ketonic acid was fermented to acetic aldehyd and carbon dioxid by means of a special ferment, carboxylase. There is a general opinion that pyroracemic acid occurs as an intermediate product of alcoholic sugar fermentation. The existing methods of affecting alcoholic sugar fermentation did not lead to a separation of pyroracemic acid, nor did Neuberg's method of fixation by means of salts of sulphurous acid, nor the dimedon method, nor a third way of fermentation, which Neuberg accomplished by undertaking the fermentation in the presence of salts which render the fermentation medium alkaline. All this only made it possible to characterize the product into which pyroracemic acid was transformed, but the occurrence of the ketonic acid itself could not be observed. In order to prove its existence, the writer looked for a method which would bring about a more radical transformation of pyroracemic acid than is obtained by the formation of salts and the above mentioned condensation reactions. Such a method was found in Dobner's synthesis, which is based upon the fact that molecular proportions of an aromatic amine (like anilin), pyroracemic acid, and of any aldehyd are condensed to substituted cinchonic acids. As according to Dobner's assertion alpha-methyl-beta-naphtocinchonic acid is produced at ordinary temperature by bringing together ethereal solutions of the original components (1 molecule each of

beta-naphthylamin, pyroracemic acid and acetaldehyd), it was necessary to work with pressed extract of yeast, as living yeast cannot support a direct contact with an ethereal solution of beta-naphthylamin. For the reaction a shaking apparatus was used. The ether was evaporated, the whole mixture brought to a small volume by heating it at 36°, and the remaining albumin destroyed by the addition of a little alcohol; then a little ammonia was added and the methylnaphthocinchoninic acid kept in solution in the form of its ammonia salt. After filtering the solution from impurities, zinc acetate was added to the solution and the zinc salt of methyl-naphthocinchoninic acid was precipitated. The free acid was obtained by decomposing the zinc salt with hydrochloric acid; it was crystallized from 50% alcohol, and then identified by its melting point, transformation into the silver salt, and lastly by transformation into naphthoquinaldin. From 180 gm. of crude sugar, 7.3 gm. of methylnaphthocinchoninic acid were obtained. This result proves the existence of pyroracemic acid as an intermediate product of zymatic sugar fermentation.

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(1b—74)

**Deaminized Protein.**

*J. Herzig and Hans Loeb, Hoppe-Seyler's Ztschr. f. physiol. Chem., 117:1, Berlin, Nov. 10, 1921.*

Deaminized glutin combines a methyl group with its oxygen and nitrogen molecule just as easily and produces the same amount of amino-nitrogen by the Van Slyke or Sorensen method as does glutin itself. These relations were studied with egg albumin, casein, and gliadin. Deaminized glutin, egg albumin, casein, and gliadin were subjected to methylation with diazomethane. The methyloxyl or methylimid, respectively, was determined; the findings were, in glutin 4.45% OCH<sub>3</sub> and 4.89% CH<sub>3</sub> on the nitrogen atom; in deaminized glutin 5.60% OCH<sub>3</sub> and 5.30% CH<sub>3</sub> on the nitrogen atom; in deaminized casein 6.78% OCH<sub>3</sub> and 4.86% CH<sub>3</sub> on the nitrogen atom; and finally in deaminized gliadin 2.61% OCH<sub>3</sub> and 4.20% CH<sub>3</sub> on the nitrogen atom. As it was formerly assumed that the free amino-group alone is important for the methylation of the nitrogen in the amino-bodies, consideration of the treated substances as deaminized derivatives has no significance in view of their easy methylation, as shown in the foregoing. As a proof of this the different deaminized proteins were analyzed by the Van Slyke method with the apparatus devised by Klein, and were studied for the content of amino-nitrogen by the formol titration method of Sorensen. The determination of the total nitrogen by the Kjeldahl method was omitted because this only attempts to obtain comparable amino values of the protein itself and of the deaminized product from the same.

The determinations were made in water, and later (in the case of slightly soluble compounds) partly in sodium hydroxid after Pauli. The following percentages of amino-nitrogen were found: In glutin solution 1.06%, in deaminized glutin 1.284-1.307%, in egg albumin 1.217-1.235%, in casein 0.966-0.993%, in deaminized casein 1.218-1.249%, in gliadin 0.287%, in deaminized gliadin 0.268-0.275%.

From these experimental data the question arises whether the deaminized compounds under investigation can still be derivatives of split protein. The explanation may be advanced that besides the resulting deamination there is also a more or less significant decomposition and an automatic rebuilding of new amino-groups.

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**Studies on Proteinogenous Amins. XII. The Production of Histamin and Other Imidazoles from Histidin by the Action of Microorganisms.**

*Milton T. Hanke and Karl K. Koessler, J. Biol. Chem., 50:131, Jan., 1922.*

The authors studied the behavior of a large number of micro-organisms on a liquid medium consisting of histidin dichlorid, ammonium chlorid, potassium nitrate, potassium dihydrogen phosphate, sodium chlorid, sodium sulphate, sodium bicarbonate, calcium chlorid, and glycerol in a total aqueous volume of 200 c.c. The organisms studied were *B. coli communior* (7 strains); *B. coli communis* (5 strains); *B. lactis aërogenes* (5 strains); *B. acidi lactici* (12 strains); *B. enteritidis*; *B. typhosus*; *B. paratyphosus A* (3 strains); *B. dysenteriae Flexner, Morgan, and Shigae*; *B. foecalis alcaligenes I and III*; *B. mucosus capsulatus* (3 strains); *B. bifidus*; *B. influenzae*, *B. proteus vulgaris* (2 strains); *B. cloacae*; *Streptococcus hemolyticus* and *viridans*; *Pneumoccus* (Types I, II, III, and IV); and *B. tuberculosis* (5 strains).

Of the 29 strains of *B. coli* (in the narrower sense) that the authors studied, 6 were able to convert histidin into histamin on the synthetic medium. Five members of the colon group (in the narrower sense) gave quantitative evidence that an alkali-stable, carboxylated triamino-compound was formed from the histidin. None of the other organisms gave quantitative evidence for the formation of such a compound; but most of them gave results that would suggest that such a compound was formed to some extent as an intermediate in the decomposition of histidin. Imidazole acetic, propionic, lactic, or acrylic acid was formed by *B. paratyphosus A* (1 strain); *B. dysenteriae Flexner, Morgan, and Shiga*; *B. foecalis alcaligenes I*; *B. mucosus capsulatus* (2 strains); and *B. tuberculosis* (4 strains). The addition of leucin to the standard medium facilitated the growth of all the organisms studied. If the organisms produced no histamin when leucin was absent, they did not produce histamin when leucin was present; but if the organisms produced histamin when leucin was absent they produced 20 to 25% more of this amine, in two weeks of incubation, when leucin was present. Leucin augments a power that already exists; it does not create a new enzymatic activity. The addition of alanin, leucin, arginin, glicin, or peptone (either Witte or Difco) to the standard medium, augments the growth of the colon bacillus and increases the yield of histamin. When glutamic acid or tryptophan are added to the standard medium, the growth of the organisms is augmented; but the output of histamin is decreased. Cystin was found to be unfavorable to the growth of the colon bacillus. The

presence of this amino-acid reduces the yield of histamin to almost nil. The addition of tyrosin to the authors' standard solution seemed to have no influence upon the rate of histamin production.

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**Studies on Proteinogenous Amins. XIII. On the Electronic Interpretation of Certain Biochemical Phenomena.**

*Milton T. Hanke and Karl K. Koessler, J. Biol. Chem., 50:193, Jan., 1922.*

In their work on biologic problems the authors frequently encountered reactions which could not have been readily explained on the basis of the accepted structural formulas of the compounds involved, because these formulas are incomplete indexes of the degree of oxidation of the carbon atoms. The authors were led, therefore, to a consideration of the interatomic forces. They found that the electronic formulas so derived were of great service in clarifying certain puzzling phenomena. Apparently yeast can hydrolyze only those acids containing quadruply positive carboxyl groups. This explains why all the alpha-ketonic acids should give an aldehyd plus  $\text{CO}_2$  as primary oxidation products, because they all contain quadruply positive carboxyl groups. Glyoxylic acid, which contains a negative carboxyl group and, therefore, could not give  $\text{CO}_2$  on hydrolysis, is practically not fermented by yeast. The fact that in the animal body the fatty acids undergo oxidation, predominantly in the beta position, suggested a causal rôle on the part of the electric structure of the molecule. The carbon atom can occur in 5 stages of oxidation, ranging from quadruply negative, through each possible combination, up to quadruply positive. It seems, moreover, that normal body cells frequently find it difficult to oxidize quadruply negative carbon. For this it may be concluded: (1) If a compound containing various forms of carbon were fed to an animal, it would be expected that the more easily oxidizable carbon atoms would be oxidized first and predominantly, and that most of the products would undergo further oxidation. (2) In diseases, such as diabetes, in which the oxidizing power of the body cells is greatly diminished, it might be expected that the quadruply negative carbon atoms which are more difficult to oxidize would be excreted with some of the partially oxidized products from the more easily oxidized carbon atoms. The excretion by diabetics of large quantities of acetone and aceto-acetic acid is well known. Examination of the electronic formulas of the fatty acids and their derivatives shows that the fact that their oxidation is predominantly in the beta position may in every case be explained by the fact that the beta carbon atom is less negative than the others.

From the principles of the polarity of a double or triple bond, of the determination of the charge on a carboxyl group, and of hydrolysis, and from a careful analysis of the reactions of the various fatty acids, new electronic formulas, the only ones which are possible in view of their chemical properties, have been worked out. Two new electronic principles have also been evolved, namely that: (1) the polarity of the double bond in an unsaturated ali-

phatic compound is determined by the electric charge on the first substituting group; and (2) a carbon atom which is attached to an oxygen atom will become at least doubly positive, when this is at all possible.

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**Studies on Proteinogenous Amins. XIV. A Microchemical Colorimetric Method for Estimating Tyrosin, Tyramin, and Other Phenols.**

*Milton T. Hanke and Karl K. Koessler, J. Biol. Chem., 50:235, Jan., 1922.*

The authors describe methods which have been devised for the quantitative colorimetric estimation of phenol, o-cresol, m-cresol, and p-cresol, p-oxyphenylacetic, p-oxyphenylpropionic, and p-oxyphenyllactic acids, tyrosin, and tyramin. These methods are based upon the fact that phenols react with diazonium compounds in alkaline solutions to give colored derivatives. A freshly prepared solution of p-phenyldiazonium sulphonate is mixed with a dilute solution of sodium carbonate. A dilute solution of the phenol whose concentration is to be estimated is mixed with the alkaline reagent which gives rise to a primary color that is yellow to red, depending upon the character of the phenol. The phenols studied can be divided into 3 classes: A. Phenols in which the para-position is not occupied by a second substituent. B. Phenols in which the para-position is occupied by a second substituent that does not contain an amino-group. C. Tyrosin and tyramin. Phenols belonging to Class A (phenol, o-cresol and m-cresol), couple with great speed and give rise to yellow colors. Phenols belonging to Class B (p-cresol, p-oxyphenylacetic, p-oxyphenylpropionic, and p-oxyphenyllactic acids), couple more slowly than those belonging to Class A. The color produced is predominantly red. Tyrosin and tyramin show an anomalous behavior toward alkaline ( $\text{Na}_2\text{CO}_3$ ) p-phenyldiazonium sulphonate. An evanescent pink color is produced at first, which fades in 30 sec. to a yellow of inconstant intensity. The simple process employed by the estimation of imidazoles and the other phenols cannot, therefore, be used for the estimation of tyrosin and tyramin. The primary yellow color produced by tyrosin or tyramin is enhanced somewhat by the addition of sodium hydroxid. The colors produced are not directly proportional to the amount of phenol present. If this strongly alkaline liquid is now treated with a small amount of hydroxylamin hydrochlorid, a very intense bluish red color is produced whose intensity is directly proportional to the amount of tyrosin or tyramin present. Tables are given for the direct determination of quantities of these phenols ranging from 0.000001 to 0.00005 gm. The amount of the phenol derivative in any quantity of liquid can then be determined, by multiplication, with an accuracy of from 0.5 to 3%.

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**Studies on Proteinogenous Amins. XV. A Quantitative Method for the Separation and Estimation of Phenols Including Phenol, O-Cresol, M-Cresol, and P-Cresol, P-Oxyphenylacetic, P-Oxyphenylpropionic, and P-Oxyphenyllactic Acids, Tyrosin, and Tyramin.**

*Milton T. Hanke and Karl K. Koessler, J. Biol. Chem., 50:271, Jan., 1922.*

Description of a method by means of which volatile phenols, aromatic hydroxy-acids, tyramin, and tyrosin can be quantitatively separated and estimated. The phenols are determined by the colorimetric process previously described by the authors. Volatile phenols, phenol, o-cresol, m-cresol, and p-cresol, are distilled off and estimated in the distillate. Aromatic hydroxy-acids, p-oxyphenylacetic, p-oxyphenylpropionic, and p-oxyphenyllactic acids, are extracted with ether from the acidified aqueous liquid which has been freed from volatile phenols by distillation. The aromatic hydroxy-acids are estimated in the ether extracts. The remaining liquid, which contains all of the tyramin and tyrosin, is made alkaline with sodium carbonate and freed from tyramin by extraction with amyl alcohol. Tyramin is then determined in the amyl alcohol extract; tyrosin is determined in the alkaline aqueous liquid. The separations are quantitative and the colorimetric determinations are accurate to 0.5 to 1.5%.

(1b—79)

**The Relation of Histamin to Intestinal Intoxication. I. The Presence of Histamin in the Human Intestine.**

*Jonathan Meakins and Charles Robert Harington, J. Pharmacol. & Exper. Therap., 18:455, Jan., 1922.*

Bacterial putrefaction possibly plays a certain rôle in complete digestion. This takes place practically entirely in the cecum and the proximal part of the transverse colon. In considering the various end-products of the putrefactive digestion, which might under abnormal circumstances exert a toxic action on the organism in general, the writers selected those resulting from the digestion of protein and, in particular, the amins which might result from bacterial decarboxylation of the amino-acids. It was decided, therefore, to seek for the presence of histamin, not because it was considered a priori that this was necessarily a causative agent of intestinal toxemia under normal conditions, but because if it were found that this and other possibly toxic substances were invariably present in the cecal contents, under abnormal conditions of structure and function, these might be proved to be operative as toxic agents. The material investigated consisted of cecal contents, contents of the transverse colon, and feces of patients in the Royal Infirmary, Edinburgh. The presence of histamin, in minute concentration, was demonstrated in the cecum (4 cases) and in the transverse colon (2 cases). The formation of histamin is apparently not dependent upon the existence of intestinal obstruction, since it occurs several weeks after the obstruction has been removed. Histamin could not be detected in the feces, whether there

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was intestinal disturbance or not. The writers regard this as probably due to the oxidation of this substance during the passage through the large intestine.

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**Chemistry of Homogentisinic Acid.**

*Carl Th. Mörner, Hoppe-Seyler's Ztschr. f. physiol. Chem., 117:67, 85, Berlin, Nov. 10, 1921.*

In boiling homogentisinic acid and ferric chlorid solutions of varying concentrations (5, 10, 25, 50%) in no case was a smell of quinon noted, wherefore it was concluded that no volatile quinon substance was formed and that this might be found in the distillate. It has been shown, however, that this is not the case. Heated ferric chlorid with homogentisin or its nearest oxidization product (nonvolatile benzoquinon acetate) yields a crystalline, volatile, chlorin-rich quinon which, owing to its unusual insolubility, can easily be isolated from the distillate. The most favorable results were obtained if 100 c.c. were distilled off from 0.3 gm. homogentisinic acid to which after the beginning of boiling 400 c.c. of 37.5% ferric chlorid solution had been added in a fractional distillation flask of 700 c.c. capacity. The yield of quinon equalled about 50% of the homogentisinic acid. The crystals resembled lead iodid. An odor of quinon was never detected. Distillation tests were made with compounds related to homogentisinic acid in the same way and with the same volume of 37.5% ferric chlorid. The distillate was shaken with ether and left to evaporate spontaneously after drying with  $\text{Na}_2\text{SO}_4$ . Homogentisinic acid lactate, benzo-hydroquinon, arbutin, toluhydroquinon, and gentisinic acid were tried, but the peculiar chlorination effect with heated ferric chlorid solution was observed only with the homogentisinic acid itself and its closest relation, the lactate and the first oxidization product (benzoquinon acetate). The crystallized substance obtained by distillation of homogentisinic acid with concentrated ferric chlorid is easily identified by known reactions and by the iodometric determination according to Valeur. It crystallizes in leaflets; its melting point is  $89^\circ$ ; it is easily soluble in ether and acetone, and it can be recrystallized from ligroin, petroleum ether and alcohol. The substance is odorless and tasteless, and sublimable, and when applied to the tongue and skin it produces a prolonged brown discolouration. Treatment with HI yields a deep golden, well crystallized derivative with a melting point of  $149\text{--}150^\circ$ .

The lead salt of the homogentisinic acid was determined crystallographically as long prismatic monoclinic crystals drawn out vertically to a symmetrical plane; the planes in the zone of the b axis, except for (100) were strongly banded  $(100):(0.01)=76^\circ 10'$ . The extinction point for Na-light was about  $(100)=10^\circ 20'$ . One molecule of water of crystallization was found. As for the lactate combination, it was shown, in opposition to Wolkow and Baumann, that when heated at  $100^\circ$  only about  $\frac{1}{20}$  to  $\frac{1}{10}$  of the anhydrols water molecule is driven off; only at a temperature of  $130^\circ$ , the loss in weight was such as to account for the complete dissipation

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of the anhydrous water molecule; at that temperature the lactate was partly sublimed. The latter is the temperature of sublimation. The solubility in water was determined at 1:1.8 at 17.5°.

(1b—81)

**A Modification of Folin's Colorimetric Method for the Determination of Uric Acid.**

*Henry Jackson, Jr., and Walter W. Palmer, J. Biol. Chem., 50:89, Jan., 1922.*

The authors record 2 important objections to the colorimetric method of Folin and Wu for the determination of uric acid. First, the relatively slight intensity of the color developed with such amounts of uric acid as are in normal blood; second, the troublesome crystalline precipitation which appears in the colored solution, thereby rendering reading impossible without filtration, a procedure which somewhat diminishes the color. The authors endeavored to find the cause for the precipitate, and observed that if Folin's uric acid reagent were dialyzed in heavy parchment membrane against large amounts of tap water, until all the free acid was gone, and the solution so dialyzed was evaporated to dryness, a reagent was obtained which, in the presence of uric acid and an excess of NaCN, gave a very intense color and a more or less dense flocculent precipitate. The latter did not alter in amount or character over a period of twenty-four hours or more. If, on the other hand, Folin's uric acid reagent were boiled cautiously to dryness without dialysis, a reagent was obtained, which in the presence of uric acid and an excess of sodium cyanid gave the same intense color, but also a dense crystalline precipitate in the course of three to five minutes. This last reagent, which the authors designate as sodium phosphotungstate "B," when mixed with the dialyzed sodium phosphotungstate "D" will cause dissolution of the flocculent precipitate; at the same time no crystalline precipitate will develop unless too much "B" is added. The proper mixture of these 2 salts results in a reagent which gives a color 5 times as intense as that given by Folin's procedure, which color increases gradually and proportionally in both standard and unknown, so that when standard and unknown are made up at the same time, they may be read at any time during the next two hours or more. No crystalline precipitate develops in the colored solution.

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**Colorimetric Determination of Uric Acid.**

*J. Lucien Morris and A. Garrard Macleod, J. Biol. Chem., 50:55, Jan., 1922.*

A colorimetric method for determining small quantities of uric acid. The reagents necessary are 2.5% zinc chlorid solution; 10% sodium carbonate solution (if monohydrated sodium carbonate is used, allowance must be made for the water of crystallization); 10% hydrochloric acid solution; 10% sodium cyanid solution; standard uric acid solution (phosphate solution of Benedict-Hitchcock). For the removal of proteins the following solutions are necessary: 10% sodium tungstate;  $\frac{2}{3}$  N sulphuric acid, within 5% by titration; solid potassium oxalate. In addition to the solutions described above, a solution of

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arseno-18-tungstic acid is necessary for this new method. The solution is prepared as follows: Boil a mixture of 100 gm. hydrated sodium tungstate, 125 gm. arsenic acid anhydrid, and 650 c.c. water for two to four hours in a flask. If the reagent so formed has a blue or green color after it has boiled the required time, it should be decolorized by boiling with sufficient bromine water to make the color a clear yellow or yellowish brown. After boiling off any excess bromine, add distilled water to make the volume 1 liter. The arsenotungstic acid reagent so prepared is a somewhat lighter color than the phosphotungstic acid reagent.

The authors' method is essentially the same when used in uric acid solutions of such different concentration as urine and blood. The procedure as used in urine is as follows: Pipette 1 c.c. of urine into a 50 c.c. centrifuge tube and dilute with distilled water to about 40 c.c. Add 1 c.c. 2.5% zinc chlorid and mix with a stirring rod. Add 1.0 c.c. 10% sodium carbonate, which should make the solution alkaline to litmus, and stir thoroughly. Centrifuge for about two minutes, drain off, and discard the supernatant liquid. Dissolve the residue, with stirring, in 3 or 4 drops of 10% hydrochloric acid, dilute with 5 c.c. of water, add 10 c.c. of 10% sodium cyanid, and transfer quantitatively to a 100 c.c. volumetric flask, and dilute to about 60 c.c. If 1 c.c. urine contains more than 0.5 mg. uric acid, the amount of cyanid should be doubled (20 c.c.) and a 200 c.c. flask used. In this case dilute to about 120 c.c. To prepare a standard containing 0.2 mg. in 50 c.c., pipette 1 c.c. of the phosphate standard solution into a 50 c.c. volumetric flask, and add 25 to 30 c.c. distilled water and 5 c.c. 10% sodium cyanid. Develop the color in both by addition of the arsено-18-tungstic acid reagent, 1 c.c. to the standard (50 c.c. flask); 2 c.c. to the unknown, if in 100 c.c. flask, or 4 c.c. if in the 200 c.c. flask. Shake, dilute to volume, let stand two or three minutes, and compare in the colorimeter. The color develops with such rapidity that the time interval indicated is sufficient if the standard and the unknown are made simultaneously. If, for any reason, they are not so prepared, it is best to allow ten minutes to elapse before making the color comparison.

The procedure as used in blood is as follows: Collect oxalated blood in the usual manner, drawing blood from a vein into a weighed flask containing 2 mg. potassium oxalate for each cubic centimeter of the sample taken. After determining the amount of blood by weight, pour it into 7 times its volume of distilled water, add 1 volume 10% sodium tungstate solution and then, while shaking, run in slowly 1 volume of  $\frac{1}{3}$  N sulphuric acid. Shake for several minutes and filter (precipitation method of Folin and Wu). Pipette 25 c.c. of the clear filtrate (corresponding to 2.5 c.c. blood) into a 50 c.c. centrifuge tube and dilute with distilled water to about 40 c.c. Add 1 c.c. 2.5% zinc chlorid, and mix with a stirring rod. Add 1.0 c.c. of 10% sodium carbonate to make just alkaline to litmus and stir thoroughly. Centrifuge for about two minutes, drain off and discard the supernatant liquid. Dissolve the residue with stirring in 3 or 4 drops of 10% hydrochloric acid, dilute with 5 c.c. water, and add 2.5 c.c. of 10% sodium cyanid and transfer quantitatively to a 25 c.c. volumetric flask. Prepare 2 standards containing 0.1 and 0.2 mg. in 50 c.c., by pipetting

0.5 and 1 c.c. of the phosphate standard solution into two 50 c.c. volumetric flasks. Add about 30 c.c. distilled water and 5 c.c. 10% sodium cyanid to each. Develop the color by the addition of the arsenic-18-tungstic acid reagent, 0.5 and 1 c.c., respectively, into the unknown and standards. If the color has been developed simultaneously, shake, dilute to volume, let stand a minute or two, and compare in the colorimeter; if not, the same lapse of time should be allowed as indicated in the case of urine. The authors claim these advantages for their method: It develops 3 times as much color per unit weight of uric acid, which color is attained with greater speed than in other methods and is more permanent as well. The use of cyanid as alkali practically eliminates the precipitation of various compounds in the colored liquid. Precipitation of uric acid with zinc salts lends itself just as well to the subsequent formation of a double radical with cyanid as in the case with silver methods. In addition there is excluded all possibility of a reduced metal giving erroneous results in the later oxidation reaction. Finally, the number of reagents required is small, they are easily prepared, and the zinc chlorid is much less expensive than the silver salts.

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**Studies on the Uric Acid of Human Blood.**

*J. Lucien Morris and A. Garrard Macleod, J. Biol. Chem., 50:65, Jan., 1922.*

By their new method of uric acid determination described in the preceding paper, the authors obtained extraordinary agreement between successive determinations in urine and blood, but marked discrepancies were observed when the values for blood were compared with those obtained by the method of Folin and Wu. As a result of their investigation of this disagreement, the authors have come to the conclusion that uric acid exists in more than one form in human blood; in this paper they furnish experimental proof that human blood contains uric acid in at least 2 forms. Many samples of blood and serum were examined for uric acid determinations by the older method of Folin and Wu and by the new method of the authors, but in spite of all precautions observed during the analyses, irregularities in the results followed. Eventually the authors decided that serum was, by nature and by quantity available, the best material for use in identifying the character of the substance responsible for the divergent uric acid values. Accordingly, specimens of human blood-serum were saved over a period of weeks and the proteins precipitated from each day's quantity of serum by the tungstic acid method. The filtrates of successive days were poured together until there was a volume of 5 liters. Several such lots were investigated after each was analyzed by (a) the method of Folin and Wu, (b) the method of Folin and Wu following oxalate, and (c) the authors' method. The tabulated results show in the case of each serum that after the process of removing uric acid from solution twice by formation of 2 different salts, the amount found present by analysis of the final crystalline product was greater than the Folin-Wu method originally indicated. This does not signify that the Folin-Wu method gives low results, but rather that uric acid is present in both forms. The Folin-Wu method

and the authors' method give comparable results when applied to standard uric acid solutions, so it must be the second form of uric acid which the Folin-Wu method fails to include, while the new method includes it. That it is some form of uric acid rather than any other substance which reacts colorimetrically may be inferred, the authors believe, because (a) it carries successively through the precipitations with zinc salt and silver magnesium mixture, which are chemically different but equally characteristic; (b) it then precipitates quantitatively upon acidification of its solution in the form of crystals which cannot be differentiated from those of uric acid; (c) it is changed quantitatively at room temperature in contact with potassium oxalate to a form readily precipitated and extracted by the usual Folin-Wu procedure; and (d) the new method gives a value for this second form, as well as the first, in spite of the exclusion of all substances so far tried, from the multiplying effect of the cyanid upon the color.

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**The Effect of Diazomethane Upon Ureids and Uric Acid.**

*J. Herzig, Hoppe-Seyler's Ztschr. f. physiol. Chem., 117:13, Berlin, Nov. 10, 1921.*

As an explanation of the power of proteins to take on methyl groups, consideration must be had not only for the free amino-groups, but also for the power of the nitrogen and oxygen to form new methyl groups. The reserve CO.NH is especially significant, since, through its tautomerism (CO.NH and CN.OH), it is adapted to form methyl derivatives with both the oxygen and nitrogen molecules. As an experimental support of this conception the relation of ureids and purin derivatives to diazomethane may be studied. The effects of diazomethane upon alloxan, barbituric acid, and diethyl, ethylphenyl and dipropyl barbituric acid were analyzed. The first two reacted readily with diazomethane. In alloxan, all replaceable hydrogen atoms, partly to the oxygen and partly to nitrogen, were methylated. No simple methyl products were obtained. On the other hand, with barbituric acid, a crystalline body was obtained in good measure; this contained a methyloxy-group besides two methylimid derivative (melting point 164°-166°). With diethyl, ethylphenyl, and dipropyl barbituric acid the results were also positive, though the power to add a methyl group to the oxygen was much less than with barbituric acid. Analysis of the results obtained in the treatment of uric acid with diazo-methane yielded tetramethyluric acid and methyloxycafein. Similar studies with cyanuric acid and biuret did not give good results. In general the results were more certain with methyloxy-determination, while there were difficulties with methylimid determination, and no certain identification could be established. They were identified by indirect means, the total content in methyl groups being obtained by analysis of the elements, and from this other methyl groups found by the methyloxy-method were subtracted. The action of dimethyl sulphate and sodium hydroxid on barbituric acid and uric acid yielded only in the first instance a beautifully crystallized product which was methyloxy-free and had a melting point of 119°-121°.

**1c. PHARMACOLOGY AND TOXICOLOGY.**

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**The Pharmacology of Oxidizing Agents. VII. Studies on the Short-Termed Production of Aortic Foci and the Mechanism of Pulmonary Edema Following the Resorptive Application of Chloramin.**

*Rudolf Jürgens, Ztschr. f. d. ges. exper. Med., 25:123, Berlin, Nov. 15, 1921.*

The most prominent symptoms of the effect of oxidizing agents are the pulmonary edema and the necrosis of the media in the aorta. The latter could not be produced with certainty by means of the chronic treatment formerly employed, as the animals soon died. A preliminary treatment with large doses of atropin (0.1-0.3 gm. per 0.5 kg. given one hour before) renders it possible to use larger doses of chlorin carriers than heretofore (0.12-0.23 gm. per kilogram in rabbits), without killing the animal during the injection; the animals remain alive for at least a few minutes. In animals treated in this way, sections show fresh focus-like injuries of the aortic media with greater regularity (about 70%), which are produced by single injections within a few minutes. The necroses are often demonstrable only with a magnifying glass or in the histologic preparation. Changes in the arrangement of the elastic fibers can be seen, and also changes in the position and staining power of the muscle cells and of their nuclei.

In order to examine the absorptive pulmonary edema which arises from chloramin, experiments were conducted on the surviving guinea-pig lung, irrigated with Ringer's solution. The amount of irrigation is not greatly influenced by the functional condition of the lung (artificial respiration or dyspnea due to irrigation with a solution of saturated oxygen), whereas a maximal distention of the alveolar walls with remedies constricting the bronchi (ergotoxin) improves the irrigation. However, this does not include the origin of a pulmonary edema dependent upon physiologic function, as it appears earlier in lungs with artificial respiration and also with insignificant increases of the irrigating pressure. There is a factor favoring edema in the normal respiratory function of the lung, in which the negative inspiratory pressure plays a part. Imidazolethylamin and ergotoxin produce diminished expansibility of the lung, but neither pulmonary edema nor vasoconstriction of the pulmonary blood-vessels; chloramin reveals no distinct vasoconstrictor effect, as soon as the concentration exceeds a certain low limit. However, below this limit a very rapid pulmonary edema sets in, which is then independent of the vasoconstriction and represents an automatic effect upon the vascular wall coördinated by it. The substance used, sodium parachloramin, is the sodium salt of paratoluolsulphochloramin.

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**Knowledge of the Effect of Hypophyseal Extract Upon the Water Economy of the Frog.**

*Fritz Brunn, Ztschr. f. d. ges. exper. Med., 25:170, Berlin, Nov. 15, 1921.*

The inhibitory effect of pituitrin on the diuresis of water, most pronounced after the drinking of pure water, is diminished with the  
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administration of sodium chlorid solutions, parallel with the concentration, so that finally a diuretic effect may appear. The hydremia arising from the inhibition of diuresis, together with the changes of concentration and amount of the urine, showed the point of attack to be in the kidney. Experiments with irrigated isolated frog kidneys suggested that the vascular area of the glomeruli was the site of the effect. Subsequent results showed that the pituitrin had no effect upon the frog kidney; experiments on animals with sutured cloaca revealed rather an increase of renal secretion. Nevertheless pituitrin is not without effect upon the water economy of the frog, which is subject to other regulatory factors in addition to that of the renal activity, as weighings after the injection of hypophyseal extract indicate. This procedure produces an increased body weight of about 28%, which does not occur under treatment with other organic extracts, and shows a specific hypophyseal effect. If the kidneys are extirpated, the frogs increase in weight; but following pituitrin there is a sudden increase of weight, so that the extrarenal point of attack is demonstrated for the frog. No positive result was obtained with drying-out experiments. A conclusion in regard to the water economy of the higher animals is not permissible at the present time.

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**The Influence of Feeding the Anterior Lobe of the Hypophysis on the Size of *Ambystoma Tigrinum*.**

*Eduard Uhlenhuth, J. Gen. Physiol., 4:321, Jan. 20, 1922.*

The author compares the size and weight of normal (worm-fed) *Ambystoma tigrinum* with those fed with the anterior lobe of cattle or with beef liver. A survey of the results shows that when fed anterior lobe these animals may reach a size far in excess of that of animals fed on earthworms, and presumably also of that of liver-fed animals. Liver produces a rate of growth as high as that resulting from anterior lobe feeding, but was found by the author to maintain growth only until the animals had reached a definite size far below that of animals fed on anterior lobe.

(1c—111)

**The Toxicity of the Blood of Adrenalectomized Frogs.**

*C. H. Kellaway, J. Pharmacol. & Exper. Ther., 18:399, Jan., 1922.*

Loewi and Gettwert, in an experiment in which the blood of a frog dying spontaneously after extirpation of the adrenals (without stimulation) was tested on the normal frog heart, obtained a slowing from 50 to 44 per minute within five minutes, and a further slowing to 40 per minute within twenty minutes. This retardation was at once abolished by atropin. In view of the possibility suggested by Dale that some substance of the type of a cholin ester (such esters being more unstable and much more active than cholin itself), might function as a hormone for the parasympathetic endings, it seemed worth while to investigate this toxic action more rigidly by perfusion experiments. Generally speaking, the serum of frogs which were either moribund or dead, as the result of adrenal extirpation, had no effect in a concentration of 1:10 upon the normal isolated frog's heart. In 1 or 2 instances slight temporary slowing was observed, but this

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effect was also obtained by a corresponding concentration of normal frog serum. In 2 cases, however, a heart block came on ten minutes after the addition of serum to the circulating fluid. Both these hearts were from large frogs, and it is possible that the restriction of out-flow through a single aortic cannula which was adapted for smaller hearts contributed to this result. In 1 case the effect was removed temporarily by the addition, to the circulating fluid, of 0.05 c.c. of 1:100,000 atropin, and permanently by the further addition of 0.1 c.c. In the other case atropin had no effect, though after washing out the system with frog-Ringer the heart reverted to its normal rhythm. The writer is not convinced that the effect of atropin in the former case is a specific, since it is not an uncommon experience to find a badly beating isolated heart improved by treatment with atropin. He believes that his experiments afford no clear evidence of the presence of any muscarin-like effect. The possible instability of the toxic substance sought for may render suspicious the perfusion experiments with the serum of frogs found dead after decapsulation, but the results were not different when the serum of animals killed when evidently moribund was at once tested on the isolated normal heart.

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**The Influence of Suprarenin on the Growth of the Tadpole.**

*Friedrich Bilski, Pflüger's Arch. f. d. ges. Physiol., 191:108, Berlin, Oct. 24, 1921.*

To determine to what extent the nervous system influences regeneration, experiments were conducted on tadpoles with different specific nerve poisons. Distinct arrest of regeneration was obtained only with alcohol, which is not explained, however, by its effects on the nervous system, but by the direct alteration of the regeneration tissue. On the other hand it was found that suprarenin accelerated growth and diminished mortality even when the solution was old, brown and, therefore, no longer active as a vasoconstrictor, though it exerted no distinct action on regeneration. A low concentration of the solution is of importance in this case. The sympathetic component of the adrenalin effect does not seem to have any bearing herein. For the present the problem of the relation between a cutaneous internal secretion and the formation of pigmentary substances rests on hypothetic considerations.

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**The Effect of Iodin and Iodothyron on the Larvas of Salamanders. IV. The Rôle of Iodin in the Inhibition of the Metamorphosis of Thymus-Fed Salamanders.**

*Eduard Uhlenhuth, J. Gen. Physiol., 4:319, Jan. 20, 1922.*

In the author's experiments 3 series of larvas of *Ambystoma maculatum* from the same brood were studied. Series 1 was fed earthworms and kept in iodin-free water. Series 2 was fed thymus and kept in iodin-free water. Series 3 was fed thymus and kept in water to which, from the twenty-sixth day on, one drop of a 1:20 M solution of inorganic iodin per 1000 c.c. of water had been added. Growth began to decrease in both thymus-fed series at an age of

nineteen days and practically ceased at an age of twenty-six days. From this time on inorganic iodin was administered to Series 3 but did not improve the growth at all. At the fifty-fourth day both thymus-fed series were divided into 2 lots and, in order to make sure that the ineffectiveness of the iodin was not due to a loss of the ability to grow, earthworms were fed instead of thymus. The result was as follows: In Series 2 the larger and stronger larvae were continued on thymus; they did not grow, and finally died at an age of eighty-two days. The smaller larvae received earthworms instead of thymus; they immediately began to grow, reached a normal size and finally metamorphosed. In Series 3 to which the iodin was administered the smaller larvae received earthworms instead of thymus; this change of the diet again resulted in vigorous growth and in metamorphosis. The larger larvae were continued on thymus, but in spite of the administration of iodin did not grow at all, until, at the eighty-second day, earthworms were used as food instead of thymus. This diet again resulted in normal growth and metamorphosis. The author, concludes that since no improvement could be obtained by iodin-administration, but immediately followed the administration of earthworms, one is justified in assuming that the inhibition of growth and metamorphosis of thymus-fed salamander larvae is not caused by a deficiency of the thymus in iodin, but by a deficiency in certain unknown substances contained in the earthworm.

(1c—114)

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**Feeding Invertebrates with Thyroid.**

*R. H. Kahn, Pflüger's Arch. f. d. ges. Physiol., 192:81, Berlin, Oct. 29, 1921.*

Larvae of nematocera (*corethra plumicornis* and *ecdurus forcipula*) and of *tenebrio molitor* were fed with thyroid or with iodobalsic acid. Whereas vertebrate larvae (amphibia) show a characteristic influence on growth and differentiation, in the present animals, only certain temporal differences in regard to growth and transformation into chrysalis and imago were observed, as compared with control animals fed with muscular substance; no characteristic differences were noted, as in the experiments on amphibia. The feeding resulted in discoloration, various degrees of brightness in the color of the skin, and slight modification of the external shape. But the metamorphosis was not accelerated, the chrysalids did not exhibit any morphologic differences, and the growth was unimpeded.

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**Irritability of the Cardiac Nerves in Frogs at Different Seasons. Contribution to the Peripheral Antagonism of the Vagus and Sympathetic Nerves, and to the Influence of Thyroid Preparations on the Cardiac Nerves.**

*Karl Cori, Arch. f. exper. Path. u. Pharmakol., 91:130, Leipsic, Nov. 4, 1921.*

It is known that the frog's vagus cannot be irritated electrically during the warm season. In the frog's vagus trunk the fibers of the sympathetic lead to the heart. Hence one must assume the interdependence of both nerves in the center as well as peripherally. The

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author, therefore, excluded the sympathetic with ergotamin, increased the vagus irritability with physostigmin and combined both. In this way he succeeded in showing that with a coil interval with which vagus irritation had no effect whatever on the summer frog, employing all 3 measures and the same current strength, diastole is lengthened immediately following vagus irritation. That increased demands of the sympathetic are responsible for the apparent nonirritability of the vagus in summer is made clear by the fact that it is possible to re-establish the preponderance of the sympathetic with adrenalin. During summer a distinct sympathetic effect can be obtained with atropin, which shows that the vagus does not cease functioning at that time. The sympathetic possesses more protracted latency than the vagus, hence the so-called positive vagus after-effect. The vagus is overcome entirely by the sympathetic only when the coil interval is small. As a matter of fact, the sympathetic effect is not suitable for quantitative experiments. In the summer a primary sympathetic effect is frequently obtained, but this is also increased by atropin (contrary to ergotamin experiment). The result of the irritation is, therefore, dependent not merely on the successful nerve, but also on the condition of the antagonist. Excess of calcium sensitizes the ventricle for sympathetic irritation, while potassium renders the heart more sensitive to vagus irritation. The blood of frogs contained actually twice as much Ca in summer as in winter. The author shows, however, that even maximal decalcification does not interfere with the vagus pause. Surplus calcium, therefore, does not sensitize the sympathetic in such a manner that the summer calcium excess could be taken to be the cause of the absence of the vagus effect. On the other hand, observations indicate the existence of endocrinous processes. During hibernation the thyroid gland is atrophied and the missing vagus effect may be restored in summer frogs by thyroid extract. The points of attack of thyroid extracts are the sympathetic nerve endings. If the sympathetic be paralyzed in the frog's heart by ergotamin, an inverse adrenalin effect is obtained, which may be again removed by thyroid products. Thus, thyroid extracts increase the irritability of the peripheral sympathetic apparatus, without themselves exhibiting any action on the heart. After irritation of the cardiac nerve trunk, following administration of thyroid, no sympathetic effect is obtained in the frog's heart. Therefore, the nonirritability of the vagus of the frog in summer might be assumed to result from thyroid atrophy.

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**The Excitation Contraction of Frog Muscle by Acetylcholin and the Antagonistic Action of Atropin, Novocain and Curare.**

*Otto Riesser, Arch. f. exper. Path. u. Pharmakol., 91:342, Leipsic, Nov. 22, 1921.*

Acetylcholin hydrochlorid possesses the property of causing contracture of frog's muscle. If the contracted muscle (suspended in Ringer's solution and describing curves under the isotonic regimen) be irritated by opening discharges from an inductor (Du Bois Raymond) it is observed that the irritability of muscle contracted by acetylcholin is not reduced. When muscle so poisoned is washed in Ringer's solu-

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tion it relaxes. The action takes place only if the acetylcholin penetrates as far as the point at which the nerve enters the muscle. Stepping the nerve produces no effect, so that acetylcholin appears to act on the "receptive substance." When muscle contracted by acetylcholin, 1:100,000, is placed in Ringer's solution containing atropin 1:1000, it relaxes immediately and on reversing the operation it again contracts. Antagonism, therefore, exists between acetylcholin and atropin. Muscle placed first in atropin and then in acetylcholin loses its power of contracture altogether. Novocain hydrochlorid, 1:1000, relaxes the muscle. Novocain, just as atropin, eliminates the contracture induced by acetylcholin. In both cases paralysis of receptive substance would seem to be the cause and this belongs, evidently, to the parasympathetic system. A nerve-muscle preparation of the frog paralyzed completely with curare reacted promptly to acetylcholin by contracture, from which it is clear that acetylcholin does not attack motor endings. If the muscle be placed for twenty minutes in curare solution its indirect irritability remains intact, but a 1:100,000 acetylcholin solution has no effect. The receptive substance is, however, irresponsible to acetylcholin before any action on motor endings has taken place. The action of curare on receptive substance is, however, rendered quickly reversible by washing in Ringer's solution. A muscle contracture with acetylcholin may be relaxed quickly by curare. The antagonism exhibited by acetylcholin and curare is in accord with the antagonism of nicotin and curare described by Langley. Tetramethylammonium hydrochlorid does not show these antagonistic effects. An adrenalin effect was not observable. Cholin acts like acetylcholin, though less strongly. Caffein and veratrin stimulate contracture by influencing muscular oxygen exchange. Acetylcholin acts on neuromuscular apparatus, causing excitation contracture in contradistinction to disturbance contracture. Acetylcholin contracture is, therefore, a type of tonic shortening. In nicotin contracture, and probably also in potassium contracture, ( $K_2SO_4$ ), 2 different parallel processes seem to be associated, viz., (1) stimulation of the receptive substance and (2) a direct paralyzing action on the contractile substance.

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**Physiology and Pharmacology of the Muscles of Leeches.**

*Werner Teschendorf, Pflüger's Arch. f. d. ges. Physiol., 192:135, Berlin, Oct. 29, 1921.*

Pieces from the skin-muscle tube of the leech which are free from centers furnish simple preparations of smooth muscles. After removing the centers, the tonus is slight, and spontaneous contractions do not occur. Mechanical stretching excites contraction; increase of temperature produces at first slight respiration (at  $33^{\circ}$ - $44^{\circ}$ ), after that slight contraction (at  $45^{\circ}$ - $51^{\circ}$ ), at the beginning of which the excitability disappears, and finally (at  $60^{\circ}$ ) heat rigor.

The electric excitability is slight; summation occurs on successive break excitations, as does fatigue with a sudden descent of the curve. The variations of osmotic pressure are so negligible that it is unnecessary to take them into account. Rhodan, iodin and  $NO_3^-$  increase the tonus; chlorin, bromin,  $ClO_3^-$  and  $PO_4^{2-}$  are inefficient anions. Lack of

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sodium ions in isotonic solution of cane sugar produces increased tonus; the effect of lithium approaches that of sodium; calcium leads to increase of tonus and in the end to necrosis. Ammonium ions raise the tonus and are poisonous. The tonus is increased by strontium and barium and lowered by magnesium; strontium stands midway between the other two. Hydroxyl ions increase the tonus; hydrogen ions have an inhibitory effect or none at all; acids may produce excitation or paralysis according to the degree of concentration and result in a speedy death of the specimens. Alcohol has a paralyzing, and ether in solution, an exciting effect; chloroform quickly kills without special excitation.

It may therefore be said that this preparation is very suitable for investigations concerning the smooth muscles of cold-blooded animals on account of its unsusceptibility to osmotic stimulation, the absence of centers, and the subtle reactions to muscle or nerve poisons.

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**Antagonism of Local Anesthetics to the Action of Veratrin on Muscle.**

*J. Schüller and F. Athmer, Arch. f. exper. Path. u. Pharmakol., 91:125, Leipzig, Nov. 4, 1921.*

It is known that the concentration of muscle induced by veratrin is attended by increased production of heat. It is not known whether it is deep-seated, or due to tetanic veratrin shortening. If very sensitive frogs' legs be placed in contact with a veratrinated muscle, as current indicators, no secondary tetanus is observed, whereas experiments with the thread galvanometer respecting oscillations gave diverging results. Such oscillations might arise from increased tonus of the supposed contractions. In that case one would expect cocaine and novocain, the local application of which eliminates increased muscle tonicity, to influence the action of veratrin antagonistically, as has been shown for alcohol and ether. For veratrination, solutions of 1:100,000, and for novocainization, solutions of 1:500 were employed. With equal irritation the veratrin effect is reduced tremendously. Cocaine, eucain, stovain, alypin, anesthesin and orthoform have a similar action. Cocaine hydrochlorid and stovain are effective even in concentrations of 1:1000. Eucain and alypin are able to eliminate only the weaker veratrin effects. The antagonism is also displayed when the veratrin effect is preceded by that of the anesthetic. The effect is reversible, in so far as the anesthetic can be washed out, when the veratrin effect is fully reestablished. The rapidity of the effect depends on the concentration of the solutions and the duration of their action. The motor nerve is not affected (no difference in the curarized muscle). The points of attack for the local anesthetics are the vegetative nerve fibers of skeletal muscles, or the contractile substance in the myoneural combination.

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**Pharmacologic Tests of the Vegetative Nervous System.**

*Stefan Rusznyák, Wien. klin. Wchnschr., 34:591, Dec. 8, 1921.*

The schematic separation of certain diseases into "vagotonic" and "sympathicotonic" is based on pharmacologic functional tests of the

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vegetative nervous system, with pilocarpin stimulating the autonomic nervous system, atropin causing paralysis, and adrenalin stimulating the sympathetic nerve endings. It is shown by these tests that in this fashion a differentiation between "vagotonics" and "sympathicotomics" is, in general, impossible; and that the hypersensitiveness to one or another of the drugs is limited simply to an individual organ. And an apparent paradox presents itself here in that without a high degree of irritability, for example, of the autonomic system, the administration of the stimulating drug gradually can become of less effect than with a state of sympathetic irritability, if the giving of the agent stimulating the autonomic system raises the, in itself, lower state of excitability of the autonomic system above the threshold. The writer obtained analogous results with a method worked out by himself, in which he employed the pupils of the eyes.

With a balanced solution of cocaine hydrochlorid (about 1%) and pilocarpin hydrochlorid (0.3-0.4%) of which 3 or 4 drops are instilled in the conjunctival sac, one obtains in more than half of the experiments no effect in the pupil, because the sympathetic-stimulating mydriatic effect of the cocaine and the miotic effect of the pilocarpin acting on the autonomic oculomotor fibers were of equal strength. Of the remainder of the cases, the majority of the patients reacted with miosis, the minority with mydriasis. Comparison with the clinical pictures showed that sensitiveness to pilocarpin was no evidence of vagotonia, and similarly, response to cocaine and adrenalin no proof of sympathicotonia. In the same individual, one organ, as for example only the eye or only the sweat glands, may show a susceptibility to pilocarpin, while other organs give an opposite reaction. It is manifest that exact functional diagnosis of the vegetative nervous system cannot be based on pharmacodynamic tests; at the most, the condition of an individual organ can be thus recognized. The conception of vagotonia and sympathicotonia as constitutional states must be given up.

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**Does Pharmacologic Action on the Vegetative Nervous System Affect the White Blood Picture?**

*H. Wollenberg, Ztschr. f. klin. Med., 92:249, Berlin, Nov. 15, 1921.*

Counts were made every ten or fifteen minutes during the first hour, and then every hour. The differentiation was by Schilling's method. In opposition to Falta it was found that a parallelism does not exist between the effect of a drug on the increase of tonus of the vegetative nervous system and changes in the blood. In one case, pilocarpin was followed by an eosinophilia; in the same case adrenalin produced a fall in the eosinophils. Perhaps for this effect of pilocarpin, which is not typical, the assumption of a special susceptibility of the eosinophilic system is necessary. Adrenalin causes a marked leukocytosis (phase 1) in which the leukocytes predominate. The type of cells squeezed out of the spleen can be of diagnostic importance (equivalent of splenic puncture). The increase of neutrophils (phase 2) may be due to their new formation. Tests with atropin cause no change in the blood picture.

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**Cholin as the Hormone of Intestinal Peristalsis. Experimental Therapy in Gastro-Intestinal Paralysis Following Chloroform Anesthesia.**

*Malte von Kühlewein., Pflüger's Arch. f. d. ges. Physiol., 191:99, Berlin, Oct. 24, 1921.*

The fact that the normal intestine contains cholin, which is the determining factor in the automatic activity of Auerbach's plexus, suggested an examination of the cholin effect in experimental paralysis plexus, an examination of the cholin effect in experimental paralysis of the cat's digestive tract obtained by deep chloroform anesthesia lasting two hours. The paralysis persists completely for two hours and is detectable even after twenty hours. Gastric and intestinal peristalsis were observed with the Roentgen apparatus following administration of potato gruel containing basic bismuth carbonate (5:25). The symptoms of this paralysis correspond entirely to those of post-narcotic gastro-intestinal paralysis in human beings. The paralysis in the cat may be cured by means of intravenous injection of 0.005-0.015 gm. cholin hydrochlorid per kg. After-effects and general condition are influenced favorably. Movements of the large intestine, which otherwise come to a standstill under chloroform anesthesia until the following day are also promoted, so that one or two evacuations take place. With slow intravenous injection no injurious influence of cholin on the animal is observed. The splitting up of cholin in the intestine is not decreased by chloroform anesthesia.

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**The Synthesis of Arsphenamin and a Study of Some of Its Intermediate Derivatives.**

*C. N. Myers, J. Lab. Clin. Med., 7:215, Jan., 1922.*

Studies were undertaken by the author in order to determine the source of toxic symptoms frequently noted after the administration of arsphenamin, and as this drug contains a small amount of arsenoxid, tests of the latter were made on rats, which proved it to be from 6 to 7 times as toxic as arsphenamin. An accompanying chart demonstrates that in preparations with a relatively high arsenoxid content, arsphenamin gives low toxicity values, and vice versa. The use of Schiff's reagent to detect the presence of free methyl alcohol, produced negative results. It was further determined that as the hydrochloric acid content varies to a considerable extent, the hydrogen-ion concentration of the finished solutions varies accordingly, providing the same amount of alkali is added in all cases. Results of experiments in connection with the relatively small quantities of the intermediate and by-products, make it improbable that they are the cause of abnormal toxicity. The author also gives descriptions of the progressive and direct methods of reducing "nitro-oxy" to arsphenamin base, as well as a process for converting the free base into the dihydrochlorid of arsphenamin. He states that at this point care is a strong factor in the purity of the final product, but that the average American product is less toxic than that formerly produced by the Germans. In conclusion Myers claims there is no apparent relationship between the degree of toxicity of arsphenamin and its arsenoxid content; that

the methyl alcohol content is too meagre to be a positive factor; but that it is highly probable that the hydrochloric acid content may be a strong factor in influencing toxicity, although further animal experimentation should be made before rendering a final decision.

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**Note on Bismuth as a Trypanocide.**

*S. Adler, Annals Trop. Med. & Parasitol., 25:433, Liverpool, Dec. 30, 1921.*

The effect of bismuth, in the form of soluble bismuth sodium tartrate in solutions of various strengths, was tried on animals infected with *T. rhodesiense* and *T. brucei* respectively. The minimum lethal dose for healthy mice was 0.047 gm. and for guinea-pigs 0.062 gm. per kilo body weight. After death bismuth was found in all cases in the liver, frequently in the spleen, and less frequently in the kidneys. The blood of a mouse was cleared of *T. rhodesiense* within twenty-four hours by a minimal lethal dose; but the mouse died in two days. A smaller dose was not effective. The drug cleared the blood of *T. brucei* (*Nagana ferox*) in guinea-pigs, but relapses occurred in a few days. A cure was never obtained.

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**The Trypanocidal Effect of Phenylglycin Amido-Arsenate of Sodium on *T. Brucei* in Rats and *T. Rhodesiense* in Mice.**

*S. Adler, Annals Trop. Med. & Parasitol., 25:427, Liverpool, Dec. 30, 1921.*

This drug is a white amorphous powder readily soluble in distilled water and yielding, in 5 and 10% concentrations, a perfectly clear colorless solution. On standing, whether exposed to light or darkness, the solution changes to a yellow color. Even daily sterilization for ten minutes was found to accelerate the development of the yellow color. Freshly prepared solutions of the drug were injected intraperitoneally into rats and mice. A table shows that no dose was toxic to the rats injected until the amount of 1.2 gm. per kilo was attained. The toxicity of the solution increases on standing. A rat, injected with 0.18 gm. per kilo of a twenty-four hour old solution, followed on the next day by a dose of 0.36 gm. per kilo of a forty-eight hour old solution, died after severe symptoms of poisoning on the sixth day after the second injection. Toxic effects of these old solutions produce, in addition to blindness and refusal of food, hemorrhages from the conjunctiva, anus and urethra. On postmortem examination, the whole intestinal tract was found to be hemorrhagic. The minimum curative dose for rats infected with *T. brucei* is 0.17 gm. per kilo of body weight. The drug has no curative effect on mice infected with *T. rhodesiense*. The minimum lethal dose is 3 gm. per kilo. No trypanocidal action in vitro was observed, either by the drug itself or by the serum of animals, twenty-four hours after they had been rendered free from trypanosomes by injections of the drug. A remarkable feature of the drug is its comparatively high minimum lethal dose.

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Toxicity of Antimony in Rabbits.

*John H. Korns, China M. J., 35:564, Shanghai, Nov., 1921.*

The use of antimony over prolonged periods as in the treatment of kala-azar is attended with potential danger. In the department of medicine, Peking Union Medical College, it has been found that the colloidal preparation does not cause untoward immediate effects even when used in doses containing an amount of antimony sufficient to produce a toxic reaction when the potassium or sodium salt is used. With a view to ascertaining the effect of long continued use of antimony and of determining which form of the drug is least toxic, the writer has injected a series of rabbits with various antimony compounds. This work indicates that when given properly the total amount of antimony which may safely be used in the treatment of kala-azar is considerably larger than has hitherto been believed. In rabbits maximum dosage within proper limits was used from the beginning without harmful results. With due regard for individual susceptibility, the writer recommends a more rapid approach toward the maximum dose in the treatment of kala-azar. In rabbits toxicity of colloidal antimony trisulphid is proportional to its antimony content, and it appears to be as toxic as the soluble salts.

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An Experimental Investigation of the Pharmacologic Activity of Drug Store Samples of Infusion of Digitalis, U. S. P. IX.

*A. Richard Bliss, Jr., J. Lab. & Clin. Med., 7:225, Jan., 1922.*

The following instructions in the Pharmacopeia, "Infusion of digitalis must be freshly prepared from the leaves," were probably based on the theory that this represents the activity of the amount of standard leaves employed. Because of this statement, combined with the many complaints concerning the unreliability of the infusion, and of the fallacy of the present-day belief on the part of many physicians, that the infusion of digitalis is a more active diuretic than the tincture or fluid extract, an investigation was undertaken on the part of the authors. For this purpose they employed the Hatcher and Brody cat method of biologic standardization. The results, shown in tabulated form, represent the theoretic activity, expressed in percentages calculated from the amounts of standardized drug supposedly used. Fifteen samples from retail pharmacies were found to contain an average activity of but 46.25% of the theoretic. Of the 15, 5 were prepared by simple dilution of the fluid extract, and the results indicated 62.6% average activity, or 24.5% more than the 10 samples supposedly prepared by the U. S. P. IX method. The 10 samples referred to possess an activity of but 38.1%. Therefore, as all samples fell much below the theoretic U. S. P. activity, attention is called to the variability of the U. S. P. infusion; to the decidedly more active infusion obtained by the dilution of the fluid extract, and also to the need for an improved method for the preparation of the infusion of digitalis. Comment is made as to the insufficiency in the amount of solvent actually employed, to the too brief period of infusion, to the

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shortage of fine powder, and to the need for standardization of the infusion. It is also stated that the present infusion of digitalis might be dropped from the U. S. P. without handicapping modern therapy.

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**Strophanthin Content of Tincture of Strophanthus.**

*L. Johannssen, Ugeskr. f. Laeger, 84:4, Copenhagen, Jan. 26, 1922.*

The method of strophanthin determination is that of G. Fromme, and depends upon the fact that strophanthin, liberated as usual by heating with salt solution, separates into strophanthidin and a sort of sugar. Strophanthidin is treated with chloroform, and after moistening, is dried and weighed. The strophanthin in the total mass is determined by multiplying by 2.178. The physiologic examination showed that strophanthin is less active than it should have been, according to the chemical determination. It may result from an envelope of glycocid. Later attempts succeeded in producing a strophanthin liberation that showed full physiologic activity. The strophanthin content of the tinctures examined varied from 0.15% (from seeds not genuine kombe) to 1.03% (Leo) and 1.07% (Gustav Lotze). The first of these was prepared from seeds bought as powder in authorized laboratories; but was probably not genuine, because it tested red with sulphur solution, while kombe seed reacts green. Santeson says that the green-reacting seeds and tinctures work more strongly for tinctures. This corresponds with the present determinations. The physiologically determined strength is about 70% of that chemically examined. All these tinctures were prepared according to Danish pharmacopeia with 70% alcohol. The preparation of the strophanthin Leo was by means of 96% alcohol. The latter showed full physiologic strength. Brauns and Closson find that kombe seed contains at least 2 kinds of glycocids, one crystalline and the other amorphous. The former by reaction with water goes over into an amorphous acid strophanthin. All 3 give the same strophanthin, but the last is only one-third as poisonous in relation to the seed. The acid reaction of the tincture of strophanthus is due to the free acid contained by the oelate of the seeds.. Conclusions: (1) Strophanthin content of tinctures varies from the proportion of 1:7 (counting those prepared from nongenuine seeds) to 1:1.9 for the rest. (2) A good tincture of strophanthus should contain 0.8% to 0.9% strophanthin, according to Fromme's method. (3) The physiologic activity of this is usually about 70% of the chemical activity. (4) A tincture prepared by cooking with 96% alcohol has the advantage that the chemical and the physiologic determinations nearly coincide.

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**The Antiseptic Properties of Acrolein.**

*A. Berthelot, Rev. d'hyg., 44:16, Paris, Jan., 1922.*

The antiseptic properties of acrolein were tested with *Bacillus coli*, *Staphylococcus aureus*, *Bacillus mesentericus vulgatus* and *Bacillus subtilis*. Although few tests were made, it appears to be evident that acrolein is not superior to formaldehyd. It is even less destructive to spores, whether used directly or by exposing the spores

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to the vapor. Its irritating effects upon the eyes and mucosae are very objectionable, even dangerous, and it cannot be employed in alkaline, soapy solutions. However, it may be possible to employ it as a fixing agent for use in the biologic laboratory.

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The Physiologic Effects of Indian Pepper (*Capsicum Pendulum*, of *Vellozo*).

*Antonino Ferrari, Rev. med.-cir. do Brazil*, 29:528, Rio de Janeiro, Dec., 1921.

A workman who was trying to strip off the seeds of Indian pepper by plunging them in water, and crushing them there, suddenly felt an intense heat, with redness and congestion of hands, spreading to his forearms; these soon became numb and heavy, and finally there was complete insensibility of the fingers, with clonic contractions, forcing him to stop work. So long as he remained standing, the movements shook his whole body, but in the sitting position these were confined to the upper extremities. The author treated the condition by immersing the arms in water as hot as the patient could bear. The myoclonia was relieved in a few minutes and, after some hours, the circulation became normal. He concludes that the pepper has an intense vasodilator effect on the arterioles of the muscles, both striped and smooth, and can hence be used effectively as a vesicant and analgesic. Internally, it may be used as a motor excitant of the unstriped fibers of the intestine or of the glands.

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The Biogenesis of Oil of Peppermint.

*R. E. Kremers, J. Biol. Chem.*, 50:31, Jan., 1922.

In studying the cohobated oils of American and Japanese peppermints grown by the Wisconsin Pharmaceutical Experiment Station, the author expected that the Japanese mint oil would be exceedingly rich in menthol, and that the American mint oil would be composed of both menthol and menthone. He based this expectation on the fact that the oxygenated constituents of an oil are usually more soluble in water than the hydrocarbons, and hence are recovered from the aqueous distillate in relatively greater quantity by cohobation. But he was surprised to find that the 1920 cohobated oil of Japanese peppermint consisted almost wholly of pulegone, and that the American mint oil, though having menthone and menthol as major constituents, contained methyl-1-cyclohexanone-3 as well. The cohobated aqueous distillate was found to contain acetone. The last 2 compounds are the products of hydrolysis of pulegone. At present the American mint is considered to be a cross between *Mentha aquatica*, Linné and *Mentha Spicata*, Hudson. The known chemical constituents of each oil and a possible scheme of their biogenesis, are tabulated by the author in his article.

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**The Active Principles of Scilla Autumnalis L.**

*Galavielle and P. Cristol, Bull. d. sc. pharmacol., 29:29, Paris, Jan., 1922.*

For clinical purposes, *Scilla maritima* (*Urginea maritima*) is employed. In the Languedoc region of France a closely related plant, *S. autumnalis*, occurs. The botanical characters are indicated. *S. maritima* is rare in France, *S. autumnalis* common. The latter should be utilized if possible. Accordingly, the plant has been examined. It is found to contain the 3 active principles designated by Merck, namely, scillipicrin, scillitoxin and scillin. The physiologic and therapeutic value of the species will be examined and compared.

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**On Scopolamin-Morphin Narcosis.**

*W. Storm Can Leeuwen and A. von Szent-Györgyi, J. Pharmacol & Exper. Therap., 18:449, Jan., 1922.*

According to Schneiderlin, 2 mg. scopolamin, or 60 mg. morphin, when given alone to an adult, do not produce narcotic symptoms, whereas half the dose of the first drug combined with half the dose of the second drug produces a narcosis of more than two hours' duration. This, then, is a case of true potentiated synergism ("Potenzierung"). This synergistic action of scopolamin and morphin does not exert itself clearly in all cases in which it has been tried in man; frequently the scopolamin-morphin combination gives unsatisfactory results in surgical cases, and sometimes death follows after relatively small doses of scopolamin with or without morphin. The writers have further investigated the matter in an experiment with 5 monkeys (*Macacus cynomologus*). They were found to be sensitive to doses of 5-10 mg. morphin, given subcutaneously, and insensitive to scopolamin. Doses of 200 mg. of this drug, given subcutaneously, did not produce any visible effect. A dose of 500 mg., given to one animal, proved fatal. Scopolamin did not augment the action of morphin on the monkeys, so far as the external symptoms produced by this drug were concerned.

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**Studies on Nonspecific Stimulation Therapy. Experimental Increase of Antianthracotic Bodies in the Blood.**

*E. G. Dresel and H. Freund, Arch. f. exper. Path. u. Pharmacol., 91:317, Leipsic, Nov. 22, 1921.*

Gruber discovered that while the blood of living rabbits and human beings is free from antianthracotic bodies, it gains these upon disintegration of the blood-plates. The authors took blood from the carotid artery in rabbits. This was digested partly as serum and partly as citrated plasma with anthrax bacilli and examined bacteriologically for its germicidal properties. Fresh blood extract and alcoholic serum extracts were also examined in the same manner. Rabbits show few antianthracotic bodies in plasma and fresh blood extract. By means of small doses of caseosan, by typhus vaccine, venesection and roentgenization, the amount of the antibodies may be increased in plasma, serum and fresh blood ex-

tract. Large doses cause their disappearance. Human serums do not contain any of these antibodies, but they may appear after intravenous injection of caseosan. In pregnant rabbits, and during the last months of pregnancy in woman, a marked antianthracotic condition is observed and the serum of untreated syphilitic individuals may contain strong antibodies of this kind. Whether the presence of antianthracotic bodies in syphilitic patients undergoing treatment with salvarsan alone, with salvarsan and mercury combined, or with mercury alone, is brought about independently of the treatment or as a result of it, remains to be determined.

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**The Disintegration of Albumin in Poisonings.**

*G. Glaubitz, Ztschr. f. d. ges. exper. Med., 25:230, Berlin, Nov. 15, 1921.*

The metabolism of albumin was studied in 12 cases of attempted suicide by means of poisons, under conditions of an accurately measured diet and bed rest. The nitrogenous content of the food was estimated and also the caloric values, according to the well-known tables. Even a slight carbon monoxid poisoning produced a distinctly increased disintegration of albumin, which lasted for a long time. Oxalic acid acts in the same way, and as a result of the tubular renal disease, the principal nitrogenous excretion sets in only after a few days. Small amounts of lysol (10 c.c.) have no effect, but larger doses (50 c.c.) show a moderately increasing effect upon the disintegration of albumin. Sublimate (1 gm.) caused a distinct increase of the excretion of nitrogen. A severe poisoning with mercuric sulphate and potassium bichromate exhibited the same effect, with a simultaneous extraordinary increase of residual nitrogen in the blood, together with a striking loss of weight. Poisoning with pantopon (1 gm.) caused a distinct increase of the albuminous metabolism and loss of weight. On the other hand, the albuminous metabolism was not noticeably changed in a case of morphinism lasting for eight years (the highest dose being 1.8 gm. per day). Toxic doses of medinal and nirvanol, also, exerted no mentionable influence upon albuminous metabolism. There are certain conditions modifying the results which are obtained in vitro from the effect of autolytic processes, due to poisoning. In part a disturbance of the supply of oxygen to the tissues is involved. The autolytic processes are antagonistically regulated by oxygen and carbonic acid; an increase in these processes expresses itself intra vitam by an increased disintegration of albumin.

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**The Pathogenesis of Carbon Monoxid Poisoning:**

*Hans Günther, Ztschr. f. klin. Med., 92:41, Berlin, Nov. 15, 1921.*

The appearance of symmetric affections is frequent. So in poisoning with carbon monoxid, there occurs not infrequently softening of both lenticular nuclei. On the other hand, polyneuritis in carbon monoxid poisoning is largely asymmetric. A patient who lay on his left side for fourteen hours in an atmosphere of

illuminating gas, afterward showed a left sided localized myositis hemorrhagica and a peculiar pigment in the urine. Tests for hemoglobin derivatives and melanin were negative. It was a question of either bilirubin or urobilin (Guenther's test). The dark brown precipitate was soluble in potassium hydroxid, insoluble in nitric acid and hydrochloric acid, and in hydrochloric acid alcohol. After neutralization with hydrochloric acid, a red pigment was extracted with ether, which gave 2 closely situated absorption bands (660-625 and 565). Besides the hemorrhagic myositis, a myocarditis was found at necropsy, to which the sudden exitus was attributed. It is firmly established that carbon monoxid has a special affinity for muscle. The effect of pressure (through the lying on the left side) appears as a contributory factor. The primary change may be caused by the splitting up of the muscle pigment, "myoglobin" being present as a respiratory pigment.

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**Blood Examination in Cases of Suspected Lead-Poisoning.**

*G. Seiffert, Münch. med. Wchnschr., 68:1580, Dec. 9, 1921.*

Stippling of the red cells is found in nearly all stages of lead-poisoning, but especially in the less severe anemic forms. This sign supports the diagnosis in the presence of others, but is not in itself a decisive sign. The presence of hematoporphyrin in the urine is another characteristic but not pathognomonic sign.

It is not difficult to demonstrate stippling of the red cells. However, it is a troublesome procedure, on account of the small number of the granules. We may speak of lead-poisoning if there is one cell showing stippling in 50 fields of the blood-smear. The thick drop method of Schwarz facilitates the search for stippling. We find suspicious cells very quickly with this method, but thinner smears should also be examined. The finding of stippling is facilitated if we do not previously fix the smear with alcohol but stain the unfixed smear with Löffler's methylene blue according to Hamel. This causes laking of the red cells and the leukocytes; granules of stippling and reticulated tissue of some of the red cells which take the stain are the only structures which may be seen. A thorough blood examination is important in lead poisoning. The technological laboratories make these examinations free of cost in Bavaria. One or two drops of blood are spread out on a slide to an area of the size of a cent and allowed to dry by moderate warmth. A thin blood smear is made at the same time. The same laboratories can make a spectroscopic examination of the urine for hematoporphyrin.

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**Mercuric Chlorid Poisoning with Recovery. A Case Report with a Note on the Urea-Concentration Test.**

*Elmer H. Funk and Edward Weiss, J. Lab. & Clin. Med., 7:233, Jan., 1922.*

A case of bichlorid poisoning with recovery, as the result of modern intensive treatment, is recorded in order to present functional studies, including the urea concentration test. Several days

following the ingestion of 4 bichlorid tablets the patient suffered from anuria. This lasted for three days, but upon establishment of excretion, he was given the MacLean and DeWesselon's urea-concentration test, which is a new method for estimating renal function. This consists of giving by mouth, after the patient voids, 15 gm. urea dissolved in 100 c.c. water, flavored with tincture of orange. Urine is passed at the end of one and two hours, respectively. Both specimens should be measured, and the second analyzed. An excretion of from 350 to 600 c.c. in two hours, with low concentration, indicates excessive fluid, but not kidney disease. If the individual can concentrate urea in the second hour specimen to 2%, or better, his kidneys are considered inefficient; if less than 2%, they are diseased.

In the present instance a marked parallelism existed between the urea concentration and phthalein elimination, coinciding with previous findings in connection with various grades of chronic nephritis. It was also noted that the blood urea nitrogen rose from 156 mg. to 171 mg. per 100 c.c. in two and one-half hours, and a similar result was noted in subsequent tests, although in fifty-one days after admission to the hospital, patient was discharged apparently well. This illustration furnishes an interesting side-light as to the comparative innocuousness of administered urea.

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**Treatment of Bichlorid of Mercury Poisoning.**

*Orville Harry Brown, J. Missouri State M. A., 19:77, Feb., 1922.*

Suicidal attempts by mercuric chlorid were formerly treated by various drugs. The new treatment consists essentially of large amounts of fluid, chiefly water, 2-3 gal. in twenty-four hours. The size of the patient governs the amount prescribed. Lemonade and orangeade, well sweetened, replace some of the water. No other treatment except sodium bicarbonate is used, unless there are special indications. The results are tremendously better than under the drug treatment. The second series contained about the same number as did the first, and presumably a goodly number had taken lethal doses of the bichlorid of mercury. The treatment with large amounts of fluid was apparently so thoroughly successful that the writer recommends it not only for mercuric chlorid but for other kinds of poisoning where the kidneys are prone to be seriously attacked.

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**The Toxic Action of Paracresol.**

*B. Vasoin, Gazz. d. osp., 43:7, Milan, Jan. 1, 1922.*

Because of its direct and intimate relation with the intestine through the circulation, the liver cannot remain unaffected when the digestive functions have been disturbed for any considerable time. Abnormal substances will be carried along the mesentery vessels to the thick part of the hepatic parenchyma, and if these contain a marked toxic power, they are capable of producing cloudy or fatty degeneration, or even necrosis of the epithelial cells, on a large scale. If these substances cons' e only a mod-

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erate poison for the organism, they will eventually provoke a productive phylogistic process, namely, cirrhosis.

To clear up certain points concerning the pathologic complex of intoxication of intestinal origin, Vasoin has, by way of experiment, made subcutaneous injections, into cats, of an aromatic sulphur product, paracresol. He notes that the blood-vessels are eventually affected by hyaline degeneration of the walls of the smaller vessels, by periphlebitis and chronic productive periarteritis, and by hyaline thrombosis. The viscera (liver, kidneys, spleen) are susceptible to sclerotic processes in probable relation to the vascular and perivascular alterations. In the liver the degenerative factors are sometimes so serious as to produce the destruction and secondary atypical regeneration of the parenchyma. The histologic signs of local hemolysis appear quite evidently and diffusely in the liver.

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### **Stamping Ink Injurious to Health.**

*Paul Borinski, Deutsch. med. Wochenschr., 47:1526, Berlin, Dec. 15, 1921.*

Report of 2 cases of intoxication in infants by means of ink containing anilin which was used in marking the laundry linen. Collapse, poor pulse, cyanosis, and a bloated appearance were noted. The clinical manifestations were those of intoxication due to anilin chlorhydrate with the copper salts in potassium dichromate, and the formation of methemoglobin as a result of the anilin poisoning. There are no objections to black anilin ink when proper directions were given. There is no certainty that the directions will be followed. It is better to use harmless ink, such as those derived from preparations of silver, in marking the linen of the infants in infant asylums.

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### **The Effect of the Poison of Tarantulas.**

*H. J. Baerg, J. Parasitol., 8:86, Dec., 1921.*

It is a rather firmly established opinion that the bite of a tarantula is fatal. Baerg, disbelieving this, decided to make a study of the poison gland and the effect of the venom. In his experiments he used a large female tarantula measuring 64 mm. from the upper angle of the basal segment of the chelicerae to the tip end of the abdomen, and 26 mm. across the cephalothorax. A 7 months' old guinea-pig weighing 635 gm. was exposed to the bite of the tarantula. Since the skin was so tough that the fangs could not pierce it, an incision had to be made on the inner side of the left leg. The tarantula struck the guinea-pig several times, but with the exception of considerable pain there were no other results noted. An albino rat, about 1 month old, was then exposed to the bite of the tarantula. The tender skin of the leg was more easily penetrated and the rat responded definitely to the effects of the poison. The responses were noted hourly. Besides a comatose condition and severe pain in the leg the rat appeared normal again in six hours. Baerg then exposed the small finger of his left hand

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to the bite of the tarantula. This was repeated several times. The results were negative excepting for considerable pain in the finger, probably a full dose of the poison was not received. The writer believes that normally the bite of a tarantula is not dangerous to man, and that even a full dose of the poison would probably not produce any very serious results, as indicated by the observations on the rat.

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#### 1d. BACTERIOLOGY AND PARASITOLOGY.

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**Yeast Nutritive Medium Made of Yeast Extract and Yeast Peptone.**

*J. Kister, Cntrlbl. f. Bakteriol., etc., 87:477, Jena, Dec. 30, 1921.*

The scarcity of meat, meat extracts and peptones during the war rendered the preparation of nutritive media in the usual way so difficult that substitutes had to be found.

Yeast, which is rich in albumin, immediately suggested itself for this purpose, as it had often been used before in the form of yeast extracts for nutritive media. A peptone was also prepared from yeast albumin, which was said to be a substitute for Witte peptone. The experiments made with yeast extract and yeast peptone gave very good results. But the pressed yeast used was frequently dark in color and poor in composition; this had a bad effect on the yeast extract and peptone. Therefore the yeast extract and peptone were prepared by the following method. The material used was a dry yeast of known albumin and extractive content. The extractives were dissolved from the dry yeast and thickened to the consistency of syrup. This was the yeast extract. In this process the true yeast albumins were coagulated. This coagulum, consisting of insoluble albuminous substances and cell membranes, was split up into water-soluble peptones by means of water vapor under pressure. The peptone solution separated from the cell remnants was changed into a pale yellow dry product in apparatus of the most modern construction. This was completely soluble in cold water and gave all the peptone reactions. This powder was the peptone which was used.

If a yeast nutritive medium of the same characteristics as the former meat extract peptone nutritive media is desired, both yeast extract and yeast peptone must be used, as the yeast extract does not contain any peptone. In the preparation of the yeast nutritive medium, it is important to have a degree of alkalinity which is adapted to the kind of bacteria to be cultivated. Yeast nutritive media prepared in the way described above, and properly alkalized, have been shown by recent experiments to equal the meat extract with peptone nutrient media of prewar days.

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**How Can Great Variations of Temperature Be Prevented in Incubators Heated by Gas.**

*Messerschmidt, Deutsch. med. Wchnschr., 47:1591, Berlin, Dec. 29, 1921.*

In laboratory incubators, just in front of the flame, where there is an automatic stop-cock, the lumen of the gas tube is so constricted by the narrowness of the opening through which it passes that, when the external temperature is very cold, sufficient gas is not admitted. To prevent this the author caused this opening to be very much enlarged. A thermoregulator guards against the flame burning too high and raising the temperature too much. Since then the temperature of the incubators does not vary more than 0.5° when the laboratory temperature is from 9 to 28° c.

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**The Influence on Spore Formation of Sealing Bacterial Cultures.**

*Laura Florence, J. Lab. & Clin. Med., 7:199, Jan., 1922.*

As a result of experiments conducted by Fabyan, in 1912, during a study of *Bacillus abortus*, it was found that successful cultures could be made by closing the culture tube with sealing wax, using a longer period of incubation. Subsequently, by this method, the *Vibrio fetus* of infectious abortion in cattle, and *Bacillus actinoides*, were discovered by Smith. Further comparisons, in 1918-19, between sealed and unsealed cultures, of some of the common sporebearers, such as *B. cerus*, *B. mesentericus coccus*, *B. mesentericus vulgatus*, and *B. welchii*, and later of *B. anthracis* and 2 unidentified bacilli, were made. Various media were employed and each tube closed by flaming the mouth of the tube and placing over the stopper a small amount of sealing wax. As this became absorbed and the tube cooled, more sealing wax was added, care being taken to avoid bubbles. By combining a few drops of methylene-blue with a medium of moderate alkalinity at the time of sealing, a reduction of the oxygen tension occurred. A table designates the kind of medium, quantity of methylene-blue, with variation of time decoloration, and a comparison of results obtained in tubes sealed hot and cold. Moisture is maintained over a long period.

In determining the time of appearance of spores, agar cultures were employed; it was found that in the sealed cultures the formation of spores was retarded, the majority of the vegetative forms of aërobies and facultative anaërobies being killed; this was not so in the case of obligatory anaërobies. The vegetative growth of the facultative anaërobies was less rapid and intense than the obligatory aërobies, but the growth of obligatory anaërobies was not apparently affected in comparison with unsealed culture tubes containing a small piece of sterile tissue. In the second sealed series inoculated from the first, spore formation was retarded a few days longer among aërobies and facultative anaërobies. Later cultures, up to 6 successive series, however, showed no variation in time appearance of spores. No uniformity in results was obtained with the anthrax

bacillus, and the rate of spore production was apparently increased by experiments with different salts. Moreover, a temporary change in the form of the bacillus was affected by the absence of a free supply of oxygen.

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**An Investigation of American Stains. Report of Committee on Bacteriologic Technic.**

*H. J. Conn, J. Bacteriol., 7:127, Jan., 1922.*

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At present it is difficult, if not impossible, to obtain Grüber stains and the American products are known to be variable. The impression always has been common that American dyes are generally unsatisfactory for staining. This investigation proved to the committee that many American stains are as good or even better than the old Grüber stains, except for certain special uses which their producers did not have in mind when preparing their products. Certain American producers of biologic stains are trying very hard to put on the market satisfactory stains. Since the stains are so essential, particularly in public health work, it is very necessary to have some dependable and standardized stains which will be domestically produced. Samples of fuchsin, methylene-blue and gentian-violet were distributed to the various investigators by number, without reference to the names of the dealers. The results of their findings are shown in a series of tables. With 3 exceptions, all the stains could be substituted for the Grüber product for fuchsin. When using it with Endo medium the Coleman and Bell Co. stain was found the best. The Coleman and Bell Co. and Heyl Laboratories produce good methylene-blue for bacilli, and good medicinal methylene-blue; 6 stand at the top, namely Calco Chemical Co., "Dealer C," Williamsburg, Coleman and Bell Co., Heyl Laboratories and the Providence Chemical Laboratories.

When the Gram stain is used as a criterion, some of the American gentian-violets and crystal-violets are as good, and some of them better than the Grüber product. By the findings of the investigators good results can apparently be counted on with any of the following stains: Methyl violet 6B, Coleman and Bell Co., Heyl Laboratories or H. S. Laboratories; crystal violet from Coleman and Bell Co., Harmer Laboratories or Providence Chemical Laboratories; and gentian violet from Coleman and Bell Co.

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**Adsorption Phenomena of Blood-Cells and Bacteria.**

*Paul Ernst, Beitr. z. path. Anat., etc., 69:152, Jena, Oct. 13, 1921.*

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When stained by Levaditi's method, the red blood-cells are studded around the edge with extremely fine black dots. Frequent examinations have shown that these adsorption borders may vary in degree. The use of colloidal solutions, such as collargol and protargol, gives excellent results, especially with fungi and water bacteria. We are dealing here not with a mere surface attraction, but with an actual penetration of the colloid solution into the bacterial or tissue cell. In this way tiny peculiar granules can be demonstrated in the bacterial cell. Neutral red and protargol (Sec. 1—Page 482)

present the same behavior. The conclusion is that the staining reaction with colloidal solutions depends upon adsorption; this is generally admitted for metal impregnations.

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**A Binocular Microscope Arranged for the Study of Colonies of Bacteria.**

*Guilford B. Reed, J. Bacteriol., 7:123, Jan., 1922.*

This binocular microscope is of great use in examining colonies of bacteria or other organisms on culture media when using direct illumination from below. Those difficulties usually encountered are obviated and observation is greatly facilitated by viewing the colonies in light reflected from the surface of the culture as is usually done when using a hand lens. The arrangement of the microscope is as follows: The tube and focusing apparatus was removed from the base and attached to a support so that its optical axis was at an angle of 45° with the stage. A 75-watt "daylight" lamp was supported 15 cm. above the stage and surrounded, except for a slit 2 cm. wide, with an opaque reflecting screen in such a position that a beam of light was projected to the stage at right angles to the optical axis of the microscope. A solid black stage provided a support for Petri dish cultures. The apparatus was of chief value in the isolation of organisms, producing very small colonies, from material containing large numbers of other species, e. g., the isolation of *B. influenzae* from sputums.

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**A New Dark Field Lamp.**

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*Falkenthal, Cntrlbl. f. Bakteriol., etc., 87:398, Jena, Dec. 17, 1921.*

A new lamp for dark-field illumination which has been tried in the laboratory has many advantages over the ordinary incandescent lamp. All disadvantages of the latter, such as high consumption of current, high candle-power, heating effect, fragility of the long, thin filaments and expensive upkeep, are eliminated. An incandescent lamp is used, the illuminating filament of which is rolled in such a way that the white-glowing spiral has a diameter of only a few millimeters. On account of the compact arrangement of the filament it is possible to obtain with a very low power (about 40 candles) the same effects in a microscope as with arc-lamps or high-powered incandescent lamps, which consume 5 to 10 times more current. To make it possible to connect the new lamp to an ordinary electric conduit, a small transformer is built into the body of the lamp. The current consumption is 20 Watts, and unlike other microscopic lamps this one works noiselessly and is free from odor. It lasts 1000 hours and can be run with tensions of 6 to 12 volts, by means of a small storage battery. It produces an almost white light resembling that of an arc-lamp.

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**Study of the Chemical Constitution of the Capsule Substance of Some Encapsulated Bacteria.**

*Eugen Kramár, Cntrlbl. f. Bakteriol., etc., 87:401, Jena, Dec. 30, 1921.*

The capsule substance of the species of bacteria thus far examined can be divided into 2 groups. The first group includes those which do not contain any nitrogen and, after boiling with dilute acids, reduce salt of heavy metals; they may therefore be regarded as polymers of different monosaccharids. The pneumobacillus is a representative of this group. In the second group the capsule substance contains nitrogen and in general is of a glycoproteid nature. Kramár studied 4 kinds of bacteria: Friedländer's pneumo bacillus, anthrax bacillus, the Bacillus radicicola and an encapsulated bacillus which he isolated from urine.

Method: The mass of culture washed from the surface of the agar with distilled water was precipitated with alcohol, washed and dried. After rubbing in a mortar, a fine powder was obtained, which, when made into an emulsion and stained with India ink, revealed the capsules around the bodies of the bacilli. The capsules were separated from the bodies of the bacilli by boiling in dilute caustic potash in which the capsules were dissolved, while the bodies of the bacilli were removed from the solution by long-continued centrifuging. The capsule substance in the solution was then precipitated with alcohol, the precipitate dissolved in distilled water and the entire process frequently repeated. The substance obtained in this way was dried, rubbed up into a fine powder, and examined.

The author came to the following conclusions: (1) The capsule substance of the pneumobacillus of Friedländer consists of galactan, and a polymeric carbohydrate resulting from the inversion of galactose. The same results were obtained with the use of ordinary agar as Toenniessen obtained from cultivation on Heim's glycerin agar. (2) The capsule of the anthrax bacillus is an albuminoid substance. As it is free from phosphorus and contains sulphur, and also a carbohydrate element which can be split off by long-continued hydrolysis, it may be regarded as a glycoproteid. (3) The capsule substance of the bacillus isolated from urine is so similar chemically to that of the anthrax bacillus that it is justifiable to assume some relationship between them. (4) The capsule substance of a strain of *Bacillus radicoccola* examined by the author was a polymeric carbohydrate which, on hydrolysis, yielded glucose and so may be regarded as dextrin.

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**Metabolism of *B. Welchii*, *Vibron Septique*, *B. Fallax*, *B. Tertius*, *B. Tetani*, *B. Pseudotetani*, *B. Botulinus*, *B. Bifermentans*, *B. Oedematiens*, *B. Aërofoetidus*, *B. Sporogenes*, *B. Histolyticus*, and *B. Putrificus*.**

*Arthur I. Kendall, Alexander A. Day and Arthur W. Walker, J. Infect. Dis., 30:141, Feb., 1922.*

*Bacillus welchii*.—*B. welchii* represents a type of widely distributed and closely related anaërobic bacilli which induce vigorous fermentation of the commonly used carbohydrates. Growth is relatively feeble in nonsaccharine mediums. Gelatin is so altered that it will no longer solidify, but this is not due to the action of a soluble proteolytic enzyme, as is the case with *B. sporogenes* and other strongly proteolytic anaërobies. The nitrogenous changes in the medium are insufficient to permit a satisfactory explanation of the phenomenon on the basis of nitrogenous decomposition. Little free ammonia is formed, but there is distinct, although moderate, increase of aminonitrogen in the gelatin medium; and it is possible that this aminonitrogen increase representing the resultant of protein cleavage by the organisms and the unused residue of this cleavage may be so related to the gelatin molecule that the latter no longer possesses the chemical and physical properties necessary to solidify on cooling. The most characteristic reaction of the gas-bacillus group is in milk. The "stormy fermentation," slightly pink color of the casein coagulum, riddled appearance of the latter, and distinct odor of butyric acid are the significant features. No other group of anaërobic bacteria so far described exhibits this cultural complex in its entirety.

*Vibron septique*.—*Vibron septique* is a carbohydrophilic anaërobic bacillus, which decomposes utilizable carbohydrates energetically with the formation of considerable amounts of titratable acid and the evolution of considerable gas, softens gelatin, but without visible evidences of energetic action on the protein of the medium, and generates gas and acid in milk cultures, the casein coagulum becoming vividly pink. The nature and extent of the visible changes in milk, however, are quantitatively distinctly less than those characteristic of the Welch bacillus, but the 2 organisms possess many points of resemblance. The cultures studied differ from the Welch bacillus, however, in their inability to ferment glycerol or starch; and their action on saccharose is distinctly less than that on the other carbohydrates studied, or is absent. These characteristics, taken in connection with the relatively slow fermentation of lactose in milk cultures, appear to be distinct points of difference between the 2 organisms. The saccharose fermenting and nonsaccharose fermenting strains apparently comprise 2 distinct types, parallel in significance to the 4 types of Welch bacillus defined by Simonds.

*Bacillus fallax*.—*B. fallax* is a carbohydrophilic organism, whose general cultural properties resemble to a moderate degree those of *B. welchii*. The fermentation of starch with the production of gas and acid differentiate from the other anaërobic bacteria, with the

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exception of the Welch bacillus, which comprise the flora of infected wounds of warfare. The relatively gradual evolution of gas, both in milk and in mediums containing utilizable carbohydrates, contrasts markedly with the rapid generation of gas in cultures of the Welch bacillus. Lactose is decomposed more slowly than the other carbohydrates, a feature of considerable diagnostic importance. The coagulum formed in milk from the slowly increasing acidity due to the fermentation of lactose is quite unlike that characteristic of *B. welchii* and *Vibrio septique*, lacking the ragged torn appearance characteristic of the former, and failing to exhibit the reddish coloration of the latter.

*Bacillus tertius*.—*B. tertius* is an anaërobic bacillus, characterized morphologically by the stainable properties of immature spores. The mature spores are terminal, and distinctly oval, a point of differentiation from *Bacillus tetani*, with which the organism might otherwise be confused; culturally, the organism is relatively inert. Its action on protein (or protein derivatives) is minimal, in which respect it strongly suggests *B. fallax*. In mediums containing utilizable carbohydrates there is a very moderate evolution of gas and an increase in titratable acidity. Acid and gas are produced from glucose, lactose, saccharose, and the hexose alcohol, mannitol; in this last, *B. tertius* is quite distinctive among the members of the carbohydrophilic anaërobic group, to which it belongs. It is distinguished from *B. welchii*, *Vibrio septique*, or *B. fallax* by its inability to use either glycerol or starch for energy, its ability to ferment mannitol, and its negative effect on nitrogenous substances.

*Bacillus tetani*.—The strains of tetanus bacillus discussed produced a soluble toxin, a very small amount of which, 0.05 c.c., would kill white mice, though no attempt was made to determine the minimal lethal dose, the sole purpose of the mouse inoculation being to establish the presence of a soluble toxin which would have a typical fatal effect on the animal. Morphologically the organisms were perfectly typical, but chemically they were relatively inert. The changes induced in the nitrogenous constituents of the ordinary cultural mediums were limited. There was a small, but definite and gradual, accumulation of ammonia, which was quantitatively the same, irrespective of the nonnitrogenous constituents, and simultaneously there was a diminution in the amount of aminonitrogen, as shown by formol titration. Gelatin was not softened, and there was no visible change in the appearance of milk. A gradual increase in titratable acidity was demonstrated in each medium, and a slow and limited evolution of gas occurred, the gas being derived presumably from some of the protein constituents. Carbohydrates were not decomposed. The cultures identified and studied as *Bacillus tetani* are not carbohydrophilic. They are feebly proteolytic. Chemically, the organisms are characterized by their relative inertness.

*Bacillus pseudotetani*.—*B. pseudotetani* is an anaërobic bacillus, morphologically similar to *B. tetani* but without toxicogenic powers. It is culturally quite inert, has no noteworthy proteolytic powers, and is almost without fermentative properties. Glucose

and maltose appear to be the only carbohydrates which it can utilize. Its principal significance lies in its close resemblance to *B. tetani*.

*Bacillus botulinus*.—The strains of *B. botulinus* studied in this series formed varying amounts of toxin which are resistant to gastro-intestinal digestion. The fermentation reactions were somewhat variable. Generally speaking, glucose and its polymers—maltose and starch—are rather more acceptable sources of non-nitrogenous energy than lactose. Saccharose was slowly fermented by 2 strains. Glycerol was fermented slowly by all. Some gas was produced even in protein mediums, and the quantitative difference in gas production and gas volume between purely protein and protein-carbohydrate mediums is not great. Considerable caution is required in the interpretation of fermentation reactions (gas production) in cultures of *B. botulinus*. The nitrogenous changes induced by *B. botulinus* in protein mediums are relatively insignificant. The organism can not be classed as a proteophilic anaerobe. Culturally, *B. botulinus* is chemically relatively inert.

*Bacillus bif fermentans*.—*B. bif fermentans* is an anaerobic bacillus exhibiting both carbohydrophilic and proteophilic characteristics. The former are indicated by a gaseous fermentation of glucose and glycerol with the concomitant development of acid and the production of a mucinous substance which accumulates in these cultures, and the latter are manifested by the formation of a soluble gelatin-liquefying enzyme with the gradual liberation of NH<sub>2</sub> groups, which are detectable and measurable by the method of formol titration.

*Bacillus oedematiens*.—Morphologically, *B. oedematiens* resembles the Welch bacillus rather closely. Milk is changed slowly by its growth, the reaction becoming acid. Ammonia is produced, except in glucose broth, in moderate amounts. Acid is produced in all mediums, but is greater in peptone mediums containing glucose. The recognition of the organism rests largely on its morphology and ability to produce a soluble poison. The rather negative chemistry differentiates it from *B. welchii* and *Vibrio septique*. The labile nature of the poison of *B. oedematiens* in contrast to the cumulative development of soluble toxin in cultures of *B. botulinus* serves to distinguish these 2 organisms.

*Bacillus aerofætidus*.—*B. aerofætidus* appears to be an organism whose primary action is proteolytic. Certain carbohydrates, such as glucose and lactose, can be utilized by it for energy, thereby reducing noticeably the attack on protein. The organism would appear to be best classified as being of the proteophilic anaerobic bacilli.

*Bacillus sporogenes*.—*B. sporogenes* belongs to the group of proteophilic anaerobic bacilli, forms a potent soluble proteolytic enzyme, which effects a relatively rapid cleavage of proteins, and utilizes protein for energy with the liberation of considerable amounts of ammonia. In gelatin and milk the amino-acid content increases materially in spite of the utilization of the products of protein cleavage, but in mediums containing protein of the peptone type the aminonitrogen content diminishes with the growth of the

organisms. The ammonia formation is of about the same rate and intensity in either type of medium. The addition of utilizable, non-nitrogenous sources of energy reduces the formation of ammonia and the utilization of amino-acids for energy.

*Bacillus histolyticus*.—*B. histolyticus* does not appear to be fermentative. In all media there is progressive increase in titratable acidity for the first few days, with a slight recession of acidity as the basic products accumulate, and coincidently a slow evolution of gas, produced in approximately equal amounts in media containing peptone and meat extractives, irrespective of the carbohydrate content. In gelatin and milk gas production is quantitatively greater, the gaseous metabolism suggesting that the origin of the gaseous products of growth is from the protein, and is not influenced by the presence of any of the commoner carbohydrates. Glycerol appears to exert no appreciable influence on the growth of the organism. *B. histolyticus* must be classed as of the obligately proteolytic group.

*Bacillus putrificus*.—The organisms identified as *B. putrificus* are plectridial anaërobic bacilli of fairly definite proteolytic properties. The fermentative properties are limited. The impression derived from a consideration of the respective proteolytic activities in peptone media, gelatin, and milk, in the order named, form a gradual progression in nitrogenous activity which would be misleading if each were considered by itself. It would appear that the milk proteins are most adapted to the nitrogenous requirements of *B. putrificus* in so far as these metabolic studies permit of comparison.

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#### The Significance and Quantitative Measurement of the Nitrogenous Metabolism of Bacteria.

*Arthur Isaac Kendall, J. Infect. Dis.*, 30:211, Feb., 1922.

Kendall discusses the nature of bacterial metabolism. The determination of total nitrogen, nonprotein nitrogen, aminonitrogen, and ammonia nitrogen, permits a fractioning or division of the nitrogen in cultural media as follows: (1) total nitrogen, (2) protein nitrogen, the difference between total nitrogen and nonprotein nitrogen, (3) nonprotein nitrogen, (4) polypeptid nitrogen, the difference between the nonprotein nitrogen and the sum of the amino and ammonia nitrogen, (5) aminonitrogen, obtained from the formol titration after subtraction of the free ammonia, and (6) free ammonia, obtained by the air current method outlined. The relations of the several fractions are indicated in accompanying tables. The least significant change appears to be that induced in the aminonitrogen fraction. More energetic proteolytic bacteria, such as *B. proteus*, induce greater changes. The aminonitrogen fraction increases but little, although the free ammonia in the plain gelatin increases very much. This increase has been shown experimentally to be due to the intracellular utilization of the protein for energy.

(1d—126)

**The Nitrogenous Metabolism of *B. Dysenteriae* (Shiga), *B. Typhosus*, *B. Paratyphosus Alpha* and *B. Paratyphosus Beta*.**

*Arthur Isaac Kendall and Reba Cordelia Haner, J. Infect. Dis., 30:225, Feb., 1922.*

*Bacillus dysenteriae*.—Although the Shiga bacillus is, chemically speaking, relatively inert, changes in the nitrogenous constituents of the mediums are clear cut. Cultures show an increase in protein nitrogen due to the growth of the bacilli, which grow more rapidly in mediums containing glucose if which the rate and extent of autolysis is somewhat less. The addition of gelatin to cultural mediums for *B. dysenteriae* has no enriching effect, the bacilli not producing any significant alteration in that portion of the total nitrogen factor which belongs to the true gelatin-protein moiety.

*Bacillus typhosus*.—The addition of gelatin to cultures of typhoid bacilli containing the usual peptone and meat extractives is of no material benefit so far as the purely nutritional value of the nitrogenous constituents of the gelatin is concerned. Whether or not the colloidal conditions of the solution are improved for bacterial growth was not determined.

*Bacillus paratyphosus alpha*.—*B. paratyphosus alpha* grows luxuriantly in both plain and glucose gelatin, there is an increase in the protein nitrogen and a corresponding decrease in the nonprotein constituents. The organism produces gas and acid in glucose mediums, but neither gas nor acid in plain nutrient broth; that is, it "ferments glucose."

*Bacillus paratyphosus beta*.—*B. paratyphosus beta* appears to multiply in a glucose gelatin medium to a greater extent with a smaller concomitant expenditure of nitrogenous substance than is the case in plain gelatin, in which both the structural and energy requirements for the entire metabolic process must be derived from the nitrogenous constituents of the medium.

(1d—127)

**The Nitrogenous Metabolism of *Bacillus Coli*.**

*Arthur Isaac Kendall and Robert S. Bly, J. Infect. Dis., 30:239, Feb., 1922.*

*B. coli* is more active, both chemically and culturally, than *B. typhosus* and members of the dysentary *bacillus* group, but in general, the nitrogenous changes produced by these organisms are qualitatively similar. The increase in protein nitrogen is also about the same, that is, the rate of growth of all the members of this series shows little variation; but the changes in free ammonia are unmistakable. In glucose gelatin there is a slight diminution of the substance, while in plain glucose-free gelatin there is a decided increase. The greater waste of nitrogen attending the growth and activity of *B. coli* in plain gelatin in comparison with dysentery and typhoid culture stands in relation to the fact that progressively pathogenic bacteria produce less deep seated changes in protein mediums than do the parasitic and saprophytic types. The fact that indol is present in cultures of *B. coli* and practically absent in cultures of *B. typhosus* is suggestive, although not conclusive evidence on this point.

(1d—127)

(1d—128)

**The Nitrogenous Metabolism of the Schmitz Bacillus.**

*Arthur Isaac Kendall, Reba Cordelia Haner, and Robert S. Bly, J. Infect. Dis., 30:245, Feb., 1922.*

The Schmitz bacillus was isolated from the feces of patients with the general symptoms of bacillary dysentery and appears to be distinguishable serologically from the Shiga bacillus and the Flexner group, although chemically it resembles the former closely. The 2 organisms can, however, be differentiated because the changes induced by the Shiga bacillus in specific constituents of nitrogenous culture medium are not caused by the Schmitz bacillus. With regard to indol formation, the Schmitz bacillus resembles members of the Flexner group, but it is differentiated from these by its inability to ferment mannitol. It is probable that the Schmitz bacillus is a distinct member of the dysentery group, not a variant of the Shiga bacillus.

(1d—129)

**The Nitrogenous Metabolism of Bacillus Alkalescens.**

*Arthur Isaac Kendall and Alexander Alfred Day, J. Infect. Dis., 30:248, Feb., 1922.*

B. alkalescens causes a rather vigorous change in reaction toward the alkaline side in plain, sugar-free gelatin. There is considerable formation of ammonia and a distinct reduction in aminonitrogen. In glucose mediums the increase in protein nitrogen is even more energetic. The substitution of a carbohydrate for the protein results in more luxuriant growth with a great saving of the protein constituents of the culture. The changes in reaction in glucose gelatin are as great, or even proportionately greater, than those in plain gelatin cultures, although of opposite sign. B. alkalescens behaves in general rather more like a parasitic than a pathogenic organism. It appears to resemble rather closely the Morgan bacillus.

(1d—130)

**The Nitrogenous Metabolism of Bacillus Proteus.**

*Arthur Isaac Kendall, Harold C. Cheetham and Cliff S. Hamilton, J. Infect. Dis., 30:251, Feb., 1922.*

The quantitative measurements carried out by the present authors on the nitrogenous metabolism of B. proteus in various mediums, and on the nature and extent of the soluble enzyme of B. proteus, confirm and extend the observations of Kendall and Walker, in the following particulars, which were specifically studied: "Bacillus proteus forms a soluble proteolytic enzyme in plain gelatin. The mature enzyme may be obtained in an active state freed from bacteria \* \* \* The enzyme appears to be a preparatory enzyme in the sense that it prepares protein for assimilation by the bacteria; it has no demonstrable rôle in the intracellular utilization of the protein by the bacteria \* \* \* The liquefaction of gelatin by the bacteria-free enzyme is not accompanied by the liberation of ammonia; deamination is an independent phenomenon associated with the intracellular utilization of the products of proteolysis by the organisms themselves."

(1d—130)

(1d—131)

Certain Genera of the Clostridiaceae. V. Studies in Patho-genic Anaërobies.

Hilda Hempl Heller, *J. Bacteriol.*, 7:1, Jan., 1922.

In a previous paper a classification was suggested for the group of anaërobic rods which include the anaërobic members of the genus "Bacillus" of former workers. The family given, was clostridiaceae, divided into 2 subfamilies, the putrificoidae, proteolytic anaërobies, and the clostridioideae, or nonproteolytic anaërobies. These anaërobies are classified according to their chemical activities, and when classified thus, they form a remarkable chain whose links one is warranted in regarding as the varied end-points of an evolutionary process. By Heller's key, previously published, it is hoped to render possible a future scientific and logical classification of anaërobic organisms. The key is briefly as follows: Under Clostridioideae, those anaërobies which do not produce  $H_2S$  demonstrable by the lead acetate paper test when grown in blood broth. The following geni under this heading do not liquefy gelatin: (1) Clostridium, Prazmowski; (2) Omelianskillus, nov. gen.; (3) Macintoshillus, nov. gen.; (4) Douglasillus, nov. gen.; (5) Henrillus, nov. gen.; (6) Flemingillus, nov. gen.; (7) Vallorillus, nov. gen.; (8) Multifementans, nov. gen.; and (9) Hiberillus, nov. gen. The anaërobies of the following geni do liquefy gelatin: (10) Welchillus, nov. gen.; (11) Stoddardillus, nov. gen.; (12) Revoltillus, nov. gen.; and (13) Arloingillus, nov. gen. Under Clostridioideae, those anaërobies which produce  $H_2S$  demonstrable by a lead acetate paper test when grown in broth, are the geni (14) Meyerillus, nov. gen., which produces a large amount of gas from carbohydrates; and (15) Novillus, nov. gen., which produces less gas from carbohydrates.

To the Putrificoideae belong the geni (16) Seguinillus, nov. gen., and (17) Regillillus, nov. gen., which produce an alkaline reaction in meat medium but do not grossly disintegrate meat particles. The (18) Robertsonillus, nov. gen., and (19) Nicollaeirillus, nov. gen., partially disintegrate the meat particles and continue to multiply in meat medium at a moderate rate for months. The geni (20) Martellillus, nov. gen., and (21) Recordillus, nov. gen., are highly proteolytic on meat medium for a short period. The (22) Tissierillus, nov. gen., (23) Putrificus, nov. gen., (24) Ermengemillus, nov. gen., (25) Metchnikovillus, nov. gen., and (26) Weinbergillus, nov. gen., are highly proteolytic, producing on three days' incubation in meat medium partial destruction of the meat particles, which continues on further incubation, till the meat particles have greatly diminished in bulk. Blackening of the meat may or may not take place.

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Influence of Different Nutrient Solutions upon the Acid Formation by *Bacterium Lactis Aërogenes*.

B. Wolff, *Ztschr. f. Kinderhk.*, 31:226, Berlin, Dec. 10, 1921.

The bacteria of the lactis aërogenes coli group produce organic acids during digestive disturbances in infants, and thus cause diarrhea and a poor utilization of carbohydrates; it is a striking fact that the large amounts of sugar recommended in infant feeding by Pirquet's school are usually well tolerated. The treatment of abnormal fer-

mentation processes consists on the one hand in a diminution of carbohydrate and the addition of albuminous preparations (plasmon, larosan), on the other hand in the supply of acid food (butter milk, albumin milk) which permits an enrichment of the carbohydrate without increasing the fermentative processes. The author has examined the behavior of nutritive food mixtures with variable cane-sugar and peptone content with reference to their modification by *Bacterium lactis aërogenes*. Nutrient solutions containing from 1 to 20% of cane-sugar and a constant amount of peptone yield approximately the same amount of acid; in solutions rich in sugar the appearance of the acid maximum is delayed. When the amount of sugar remains constant and the peptone changes, the acid formation increases corresponding with the amount of peptone. In whole milk with an addition of from 12-17% sugar, there is a diminution of the acid formation, with increasing carbohydrate content.

An explanation for this peculiar fact may be found in the assumption that there is an inhibition of ferment action when a certain degree of acidity has been reached. When *Bacterium lactis aërogenes* is planted upon butter-milk, concentrated and ordinary albumin milk with the addition of from 0-17% carbohydrates, no increased acidity results because of the high initial acidity. If these solutions are brought to the degree of acidity of whole milk by the addition of alkali, they are fermented to about the same degree of acidity as whole milk. That is, a high initial acidity of butter-milk and albumin milk prevents a further production of acid, without changing the growth or the biochemic behavior of the bacteria. Hence there exists a discrepancy between clinical and experimental findings regarding carbohydrate and albumin content, and an accordance in reference to the acidity of the food. These differences are due to the changes with regard to the acid formation, caused by the action of the body upon the relations between bacteria and food. In sick infants there is diminished secretion of gastric juice, the organic acids can develop to a certain degree, but are neutralized by the intestinal juices; in this way there never occurs any inhibition of fermentation. The albumin action in the body is explained by the fact that the albumin decomposition products are the strongest stimulants of the secretion of digestive fluids; the fermentative action of the bacteria is subordinated. The acid in the prescribed diet is usually lactic acid which but slightly stimulates peristalsis and replaces the disinfectant action of hydrochloric acid. Consequently, carbohydrates may be fed in acid mixtures without fear that they will be fermented in the absence of free hydrochloric acid, thus markedly improving their chances for absorption.

(1d—133)

(1d—133)

A Toxin-Producing Anaërobic Isolated from the Larvas of *Lucilia Caesar*.

*Ida A. Bengtson, Pub. Health Rep. (U. S. P. H. S.), 37:164, Jan. 27, 1922.*

The presence of an anaërobic organism producing a soluble toxin has been demonstrated in material consisting of 3 chickens with limb-erneck, a guinea-pig and larvae of the green fly, *Lucilia caesar*. The

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material after culture was found to be very toxic when introduced intraperitoneally into mice. Its behavior was similar to the toxin of botulism, but it was not neutralized by either Type A or B antitoxin. The organism is apparently nonproteolytic in meat mash mediums but produces a large amount of gas, these bubbles being sometimes the only evidence of growth. In smears made from twenty-four hour cultures the organism appears as a slightly curved rod with rounded ends usually occurring singly or in short chains. Spores appear in meat mediums in forty-eight hours. The organism requires anaerobic conditions in mediums not containing meat. Growth was obtained from seven day cultures heated in the Arnold sterilizer for one-half hour at 93°-195° C. but not from those heated for one hour. In the animal tests the most striking feature, as in botulism, is the marked congested condition of the blood-vessels of the brain and meninges.

(1d—134)

(1d—134)

**Studies on the Influence of Hydrogen-Ion Concentration on the Growth of, and Toxin Formation by Tetanus Bacilli.**

*R. G. Dernby and B. Allander, Biochem. Ztschr., 123:245, Berlin, Nov. 5, 1921.*

Experiments were undertaken to determine the most favorable conditions for the development of tetanus bacilli and the production of toxin, and what influence hydrogen-ion concentration exerted on the same. Tetanus strains of Danish and English origin were employed in the form of forty-eight-hour agar or broth cultures. Owing to the action of hydrogen-ion concentration on the nutrient substrate during sterilization, accurate adjustment had to be effected after sterilization. The growth was indicated by the figures 0, 1, 2, 3, 4, where 0 denoted no growth and 4 abundant growth. For testing the toxin white mice were employed, .01, .001, and .0001 c.c. being injected. If a mouse that received an injection of  $\frac{1}{100}$  c.c. showed no signs of tetanus, the agent was described as  $^{\circ}$  toxin. Hydrogen-ion concentration was determined colorimetrically and electrometrically. The examination comprised the growth of tetanus bacilli under different hydrogen-ion concentration and the changes in hydrogen-ion concentration of the substrate induced by tetanus bacilli. In general the optimum for the growth under different hydrogen-ion concentrations was fairly wide, but good growth does not run parallel to good toxin formation. Many factors are capable of destroying toxin, the foremost being sunlight, acids and alkalies. Therefore, the isolation of the toxin at different hydrogen-ion concentrations was studied. The following conclusions were reached. Tetanus bacilli grow in the comparatively broad zone of the hydrogen-ion concentration pH=5-8.5. The growth optimum lies in pH=7-7.6. The stability zone of tetanus toxin lies between pH=5.8-8, the optimum in pH=6-7.5. With a pH value lower than 5.8 (in acid medium), rapid, complete and irreversible destruction of toxin sets in, while with the higher value pH=7.5 the destruction takes place gradually. For the preparation of toxin on the large scale the initial pH is to be 8.

If the medium, on being tested after two days, shows a lower value than pH=6.8 (it must not become acid) renewed alkalinization is necessary.

(1d—134½)

(1d—134½)

**Artificial Virulence and Chemistry.**

*Bachmann, Münch. med. Wochenschr.*, 68:1589, Dec. 9, 1921.

A previous report has been given of animal experiments in which it was possible to render the injection of harmless saprophytes virulent by the coincident injection of 0.1-1% lactic acid. These experiments were performed on guinea-pigs and mice. The author attempted to corroborate the findings, but his results were all negative. Guinea-pigs used in performing the experiments in the manner described for tests with *proteus vulgaris*, *proteus X* 10 bacillus, hay bacillus, typhoid bacillus and Shiga-Kruse bacilli did not die. The same negative result was obtained in mice injected with a pure culture of *mycoides* and typhoid bacilli. It is possible that Much obtained his results as a result of some special biologic property of his cultures, which he obtained after the addition of the lactic acid.

We must suppose that the animals in Much's experiments died as a result of other and accidental causes, as long as there are no autopsy reports.

(1d—135)

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**The Relation between Fatigue and the Susceptibility of Rats Toward a Toxin and an Infection.**

*Ella Hutzler Oppenheimer and Reynold A. Spaeth, Am. J. Hyg.*, 2:51, Jan., 1922.

The experiments undertaken were to discover whether a state of fatigue will produce in experimental animals a greater susceptibility to toxins and infections. Fatigue is used in the sense of temporary exhaustion produced by excessive muscular exertion. Throughout the experiments white and hooded rats were used; the results contradict the popular belief that a fatigued individual is more susceptible to disease (tetanus toxin and pneumonia infection) than a nonfatigued individual. Fatigue was produced artificially by forcing the rats to run in a motordriven drum, the complete apparatus consisting of 6 drums belted in parallel, 2 sets of reducing pulleys, a motor, and rheostat, similar to the apparatus used by Richter. An animal was considered exhausted when it could no longer run and rolled on its back and was carried about by the drum and in general failed to respond to auditory or tactile stimuli and was content merely to lie and rest.

The minimum lethal dose of tetanus toxin for rats is 0.00000004 gm. per gram weight of rat. The results of the experiments to test the effects of fatigue on susceptibility to tetanus toxin showed that fatigue apparently tends slightly to increase their resistance to subcutaneous injections of tetanus toxins. This occurs whether fatigue precedes or follows the injection of the toxin. White and hooded rats, up to 185 gm. in weight, are not susceptible to diphtheria toxin in doses as large as 2 c.c. The

same method of procedure was used in the experiments to determine the relation between fatigue and pneumococcal infection. Eighteen-hour broth cultures of a virulent organism of Type 1 pneumococcus dilated to the desired strength with sterile broth was used. The injections were made intraperitoneally. The results substantiated previous experiments in that they proved that fatigue definitely increases the resistance of rats to this particular infection.

(1d—136)

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**The Production of Foot-and-Mouth Disease in Guinea-Pigs by Means of Pure Cultures of the Organism Causing It.**

*Max von Niessen, Urol. & Cutan. Rev., 26:85, Feb., 1922.*

The author takes the blood as the starting point for the isolation of cultures of the contagium; from it, as well as from 2 samples of Loeffler's immune serum the cultivation proceeded easily, since the contagium is free from nosoparasites in the circulating blood. The isolation was effected from the saliva and the contents of aphtha blebs. The isolation is very troublesome because the successive and elective parallel culture series easily lead to blind alleys, owing to the occurrence of identical forms, whose identification is impossible in every strain and germ which resembles it culturally, so long as elective cultural and staining methods are unknown. This is especially difficult because the contagium of foot-and-mouth disease has a polymorphic generative form cycle with metachromic properties. The utilization of fresh material has enabled the author to make pure cultures of the bacterium, which he believes to be specific for this disease, and also to corroborate the opinion that the contagium of foot-and-mouth disease of cattle is identical with, or similar to, the contagium of human venereal disease, especially the gonococcus type. The author gives the protocols of a positive experiment of transferring the disease to a guinea-pig by means of pure cultures of the organism from the blood of a beef in the florid stage of the disease.

No precise conclusions can be drawn from the experiment in regard to the period of incubation of the hematogenic, artificial infection of foot-and-mouth disease with pure cultures. After subcutaneous inoculation, it varies from two days to several weeks, depending upon the amount, virulence, stage of degeneration and age of the culture. The period may be shorter after intravenous application. However, it was shown by this experiment that not all animals, even of the same species, are sensitive to infection, or that pathodynamic differences of the individual stages of vegetation exist. The course of the eruption was in cycles, a fact which may have been due to increased superinfection, starting with relatively small amounts, in which there was no evidence of active immunization. It would seem probable that there was a cumulative anaphylactic influence.

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**A Comparative Study of Bovine Abortion and Undulant Fever, from the Bacteriologic Point of View.**

*Z. Khaled, J. Hyg., 20:319, London, Dec., 1921.*

Khaled undertook this study for the purpose of further elucidating the relationship of *B. melitensis* and *B. abortus*. The cultures used in the research were supplied by the National Collection of Type Cultures and were representative of strains isolated in America, on the Continent and in England. The morphologic, biochemical and cultural characteristics which are detailed in the text prove that *B. melitensis*, *B. abortus* and *B. paramelitensis* are undistinguishable and identical. Since the same strain may show bacillary, coccobacillary or coccoid forms from time to time or the 3 forms may occur together in the same culture, the term "micrococcus" is inexact and the more satisfactory generic name would be "brucella."

The mode of infection of cattle abortion and undulant fever is described. The two diseases present the picture of a bacteremia, with a close similarity in the modes of infection, and of excretion of the causal organisms. Immunologic tests were used. The agglutination reaction gave no means of differentiating the organisms. The absorption tests proved that when an antimelitensis serum is absorbed with *B. melitensis*, all agglutinins for *B. melitensis* and *B. abortus* are removed. The same result was obtained when *B. abortus* was used to absorb an antimelitensis serum. Anti-abortus serum absorbed with any abortus strain lost all agglutinins for both *B. melitensis* and *B. abortus*. Anti-abortus serum absorbed with *B. melitensis* had lost its power to agglutinate *B. melitensis* strains but still agglutinated *B. abortus* to full titer. These results make it appear that *B. melitensis* is a sub-strain of *B. abortus*. Experiments for the relative pathogenicity of these 2 organisms were carried out. Khaled points out that 25% of the milch cows in England are infected with *B. abortus*, and this percentage is even higher on the Continent and in America. These bacilli are found even in "certified milk." The procedure of the tests on guinea-pigs and goats is detailed. Dose for dose *B. abortus* is much less virulent for the guinea-pig than *B. melitensis*, approximately 1:6. An experiment of cross immunization showed that immunization of monkeys with killed suspension of *B. abortus* protected against subsequent infection with *B. melitensis*.

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**Viability of the Colon-Typhoid Group in Carbonated Water and Carbonated Beverages.**

*S. A. Koser and W. W. Skinner, J. Bacteriol., 7:111, Jan., 1922.*

For many years investigators have worked with the destructive effect of carbon dioxide on various microorganisms and the value of carbonation for the preservation of foods and beverages. This investigation was undertaken to determine the length of time one may expect the various members of the colon-typhoid group to withstand the environment of the different types of commercial carbonated beverages. In the writers' experiments the beverages (Sec. 1—Page 496)

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were prepared and carbonated under commercial conditions as far as possible. Control examinations of the product were made previous to experimental inoculation to determine the absence of the particular type used in the investigation. Commercial CO<sub>2</sub> was used for carbonation. Suspensions of the various organisms in sterile tap water was used for inoculation. Equal amounts of bacterial suspensions were added to each bottle before carbonation with the cultures of *B. coli*. With *B. typhosus* and *B. paratyphosus* B the samples were prepared in the usual manner and stored at 1° C. for several days, when they were reopened and the culture inoculated. In all cases plate counts were made immediately after inoculation and at definite intervals.

A series of experiments showed the marked influence CO<sub>2</sub> had upon the death-rate of organisms, which were killed at room temperature, 19° to 23° C., but less readily at 1° C. Carbonation was found to exert a distinctly harmful effect upon the members of the group; their period of viability in carbonated water is much shorter than that in plain tap water. The organisms were killed speedily, even in water saturated with CO<sub>2</sub> and not under pressure. The colon bacillus is killed much more speedily in the acid-containing beverage, the effect being especially marked at the higher temperature. In one experiment plain noncarbonated tap water was substituted for the carbonated water in the acid beverages and the death-rate of *B. coli* was practically the same. Thus, added acids produce death of the organism irrespective of CO<sub>2</sub>. *B. typhosus* and *B. paratyphosus* B are more speedily killed by CO<sub>2</sub> than is *B. coli*. The spore forms of *B. mesentericus* and *clostridium sporogenes* were found to be quite resistant to carbonation, surviving one month at room temperature with no diminution in numbers.

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**Further Results on the Isolation of Organisms from Feces by a New Method.**

*E. Wordley, J. Hyg., 20:360, London, Dec., 1921.*

The Dudgeon method for isolating organisms from feces and sputum was applied to artificial mixtures of feces with *B. typhosus*. Browning's brilliant green enrichment method was used for comparison; 100 stools were examined by the two methods. The method of procedure was as follows: Feces were collected in small sterile pots from patients with no symptoms of intestinal disease. Teaspoonful of sample was mixed with sterile saline to make a thick emulsion. Then 3 drops of an emulsion of *B. typhosus* was added. To each of 2 brilliant green tubes was added 1 loopful of the well-mixed feces and typhoid bacilli. The tubes contained 5 c.c. peptone water to which was added respectively 0.1 c.c and 0.2 c.c. of a 1:10,000 solution of dye (Grübler's). The remainder of typhoid-feces mixture was subjected to the dry method; the dry powder was spread over plates. The peptone water brilliant green tubes were incubated at 37° C. for twenty-four hours and then plated; after incubation of plates for twenty-four hours, suspicious colonies were picked off, the dry powder plates were treated similarly. MacConkey's lactose neutral red bile salt agar and litmus

lactose agar were used for plating. Tables show the positive results of the tests. Of the 100 specimens examined there were 27 positive results by the dry method and 5 by the brilliant green. The litmus lactose agar gave better results than the MacConkey's medium by the dry method. In the use of this agar there is a disadvantage, for if the plate is heavily inoculated with feces, so much acidity is produced that all colonies appear red from diffusion of the dye, and colonies of *B. typhosus* have to be recognized by their characteristic macroscopic appearance apart from any special color of the colony. Wordley has found this method superior to all others. By using it in sputum plating, a much better separation of colonies is secured. It effects a great saving in culture media, since it is a method that is equally applicable to any infection or for the isolation of any organisms that may be present in feces.

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**The Biology of Dysentery Bacilli. The Mode of Action of Disinfectants and of Starvation upon Bacteria.**

*Braun and Gersbach, Ztschr. f. Immunitätsf. u. exper. Ther., 33:247, Jena, Dec. 7, 1921.*

It was shown in typhus proteus bacilli, in typhoid bacilli and paratyphoid B bacilli, that under the influence of certain disinfectants, such as carbolic acid, thionin, Capri blue, trypaflavine, or under conditions of deficient nutrition, these bodies lose certain agglutinogens and differ morphologically from bacteria grown on rich culture media, in that no flagellae can be demonstrated. Their resistance to disinfectants, and their animal virulence, remained unchanged. Since the loss of certain agglutinogens went hand in hand with the disappearance of flagellae, it seems not unreasonable to assume that the lost agglutinogens were produced by the ectoplasmic flagellar substance. Certainly flagellae are not essential organs. Such experiments appear to be of importance, from a practical as well as from a theoretical standpoint. Immune serum which acted strongly upon bacteria abundantly supplied with flagellae was not necessarily as active toward the "starved" bacteria developing in the infected organism and showing a different structure. It may therefore be that, for the manufacture of vaccines for active immunization, and of curative serum, "starved" bacteria may be more suitable than bacteria grown upon media rich in nutritive bodies.

In the present experiments a pseudodysentery bacillary strain, H, was used, and was transferred daily to fresh agar rich in nutrient, to agar medium deficient in nutrient (starvation medium), and to carbolized agar. It presented the same morphologic changes from the original strain that proteus, typhoid and paratyphoid bacilli had shown under the same conditions. Under the influence of carbolic acid, the pseudodysentery bacillus grew to giant threads of variable shape. A differentiation of the giant forms of the carbolic strain into nucleus and cell protoplasm could not be effected with intravital staining after fixation by Heidenhain's iron-hematoxylin. The carbolic strain showed a reticulated structure which the original strain and the starvation strain do not show. The

starvation strain is characterized by its very small size and by bipolar thickening of the cell protoplasm. When fixed by heat, the carbolic strain is decolorized by Gram's method with more difficulty than is the original or the starvation strains. With intravital staining, methylene-blue, fuchsin and Victoria blue penetrate the bacteria of the last 2 strains much more readily than they do those of the carbolic strain. Disinfectants like carbolic acid and bichloride revealed no difference in their action upon the 3 strains. The carbolic strain was more resistant than the other 2 to the weak bactericidal action of methylene-blue.

In experiments to test the infectivity and the toxicity for mice, no difference could be found in the 3 strains, if emulsions of the same density were used. Agglutination tests showed no difference between the carbolic or the starvation strain, on the one hand, and the original strain, on the other. This is in direct opposition to the findings obtained with typhoid and paratyphoid bacilli. Dysentery bacilli are nonflagellate. They do not contain any body substances of agglutinogenic nature which, during starvation, can act vicariously for the flagellae, that is to say, we are dealing here with conditions differing from those in the case of proteus, typhoid and paratyphoid bacilli, which lose special agglutinogens when they lose their flagellar apparatus, because the nutritive material necessary for its elaboration is under unfavorable conditions consumed for the essentials of bacterial life. From this it may be concluded that in the latter types of bacteria the antigens lost under adverse conditions are contained in the ectoplasmic flagellae.

The morphologic changes appearing under the influence of carbolic acid somewhat resemble those of a spore. This is due to the greater density of the protoplasm of the carbolic strain, and to a thickening of the cell membrane. Bacteria stain and decolorize with difficulty, and are more resistant to the bactericidal effect of methylene-blue. These changes in the morphology of the carbolic strain must not be regarded as degeneration or involution forms, since they represent appropriate defensive actions against injurious agents. This is further evidenced by the regeneration tests, for the morphologic differences disappear as soon as the carbolic and starvation strains are cultivated under normal conditions.

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**Effect of Beef Bile on Bacteria of Dysentery.**

*Maximilian Knorr, Cntrlbl. f. Bakteriol., etc., 87:339, Jena, Dec. 17, 1921.*

Upon examining some blood samples it was found that beef bile was an excellent nutrient medium for dysentery bacteria "Y." The writer undertook experiments to find out how other species of dysentery bacteria behaved when cultivated on bile. It was found that the bactericidal power of bile varied with different species of Shiga-Kruse bacteria. The culture is always killed if started with a small initial number of bacteria, but when started with a larger amount, it usually flourishes. As in the case of true dysentery, only a small number of bacteria are present in the blood, there is only small hope for obtaining a culture of Shiga-Kruse bacteria

upon bile. Upon pseudodysentery macteria A, D, H, bile also acts bactericidally, but not to such a degree as upon Shiga-Kruse bacteria. But dysentery bacteria "Y" flourish upon bile; after six hours the number of organisms has quadrupled. Therefore, culture upon bile gives an experimental explanation of the twelvefold increase in numbers of these bacteria in circulating blood. The amount of bacteria of this species is increased in the blood by beef bile. Further it also explains the presence of "Y" bacteria in the intestine when not accompanied by conspicuous anatomic changes, although such changes are favorable for a more numerous and prolonged existence. These investigations strengthen Ruge's assumption that it ought to be possible to influence favorably the course of Shiga-Kruse and pseudodysentery by bringing about a copious secretion of bile; the results might also explain the effects of ipecacuanha and calomel in cases of true Shiga-Kruse dysentery, and the nearly related pseudodysentery, as these preparations help to stimulate bile excretion. Therefore, it is advisable in such cases to use bile therapeutically, particularly during the initial period of the disease and during convalescence, and not only to use preparations which stimulate bile excretion but to make injections of animal bile.

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**The Bactericidal Action of Rabbit Bile on Certain Strains of Streptococci.**

*Ruth L. Stone, Am. J. Hyg., 2:67, Jan., 1922.*

Stone undertook a number of experiments to determine the bactericidal effect of rabbit bile on *Streptococcus pyogenes* and other members of the streptococcus group. The pneumococcus is the only human pathogen on which rabbit bile has a nocuous effect. The action of bile on *S. pyogenes* is not lytic. Bile from various rabbits, both normal and immune to streptococci, was tested with this strain with the results that 0.01 c.c. of bile killed a twenty-four hour culture; only occasionally a scant growth appeared in the 0.1 c.c. dilution, but never in any greater concentration. Horse, sheep, beef, dog, cat, turtle, guinea-pig, and human bile exert no inhibitory action on any of these strains of streptococci. A table shows that every strain of *S. pyogenes* tested, regardless of source, was killed by the action of rabbit bile. This effect was not noted upon any of the nonhemolytic streptococcus strains: 6 out of a total of 14 strains of *S. viridans* were unaffected, the results are as yet unexplainable. Out of about 70 different aërobies, 8 were killed by rabbit bile. The following tests were made to determine whether the bile was absorbed by the bacteria: The smallest amount of bile which would kill 0.1 c.c. of culture was determined; 10 c.c. of this dilution of bile was made up and the corresponding necessary amount of culture added. This mixture was incubated for twenty-four hours and then centrifuged. The sediment was plated and gave negative results. The supernatant fluid was used again and all the plated cultures were negative. This proved that death is due to mere contact and not absorption or adsorption. Repeated autoclaving does not diminish this bacteri-

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cidal power. Alcoholic and etherial extracts were made and the bactericidal substance was found to be located in the alcohol-soluble, ether-insoluble fraction of rabbit bile.

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**A New Culture Medium for Diagnosis and Culture of Streptococci in the Circulation.**

*Gerhard Piorkowski, Deutsch. med. Wchnschr., 48:69, Berlin, Jan. 12, 1922.*

The results of the American author Fischer were examined. The work was relative to insidious streptococcal infection of the mouth which, in the presence of lowered resistance, leads to endocarditis, polyarthritis rheumatica, osteomyelitis juvenilis, pericarditis, icterus with no Weil's spirilli, and other conditions. Streptococci appeared in from twenty-four to forty-eight hours, were apparently well nourished and were recognized by other means. The culture medium was made as follows: To 5 c.c. 1% grape-sugar bouillon with 2% peptone and 1 c.c. 2% solution dried egg albumin (tap water), was added a 20% solution N/10 NaOH. It is especially important to have the reaction alkaline, to neutralize the grape-sugar bouillon.

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**The Nutrition of Acid-Fast Bacteria.**

*Esmond R. Long, Am. Rev. Tuberc., 5:857, Jan., 1922.*

The author reports a series of 450 culture experiments made in the interest of a definite classification of bacteria. He questions the propriety of herding together some 40 types of microorganisms and placing them in a bacteriologic classification, known as the "acid-fast" group. His tabulated report of experiments to date furnishes a start in classification and lays the foundations for a few broad generalizations. He believes that if the classification is to be useful in a practical way it must recognize the point of view of parasitism as against avirulence. One of the characteristics of saprophytes as seen in the uncontrolled conditions of nature is their ability to break down complex into simple compounds. Complex chemical groupings such as benzene and indol rings are torn to pieces, the amino grouping is vigorously attacked by saturation with water, and ammonia is split off from stable groups like amines. In a general way parasites are more helpless, and more likely to thrive on nutriment, a portion of which at least is pre-digested; many of them are prone to leave untouched undigestible morsels like the aromatic rings. The alcohols, other than glycerol, and the organic acids used, are insufficient sources of carbon for the tubercle bacilli. They must have something more, preferably glycerol. They are thus at once set apart from this heterogeneous group, which uses these substances to a varying degree.

Turning to some of the characteristics of saprophytism, the author notes that the complex imidaxolpropionic structure (histidin) is utilized by smegma and grass bacilli as a source of carbon and useless to the others. Something like the same separation can be made on the basis of the utilization of the nitrogen of the com-

plex tryptophane. Utilization of the creatinin imino nitrogen and abstraction of nitrogen from urea again places the smegma bacilli with the grass bacilli and both of them apart from the tubercle bacilli. After exclusion of these 2 extremes, there remain the leprosy bacilli, provisionally so-called, with due recognition of their insecure etiologic status, and the bacilli of cold-blooded animals. In their utilization of the carbonaceous portions of d-l-alanine leucine, these behave somewhat alike and more like the grass and smegma bacilli than like the tubercle bacilli. In their less general utilization of propionic and lactic acid and ethyl alcohol as sources of carbon, they act more like the tubercle bacilli. In their action on creatinin they are again more like the grass bacilli. In their failure to use the carbonaceous part of histidin they behave similar to, and resemble more, the tubercle bacilli.

It will be seen that the tubercle bacilli and the smegma and grass bacilli fall readily into separate nutritional groups. The lepra and cold-blooded animal bacilli have many points of difference from both of these and certainly a few nutritional factors in common. Tentatively they can perhaps be considered together as a third group. Finally it should be added that the distinction between human and bovine types of tubercle bacilli has so far proved too subtle to be drawn on a nutritional basis.

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**The Griffith Method for the Direct Isolation of Tubercl Bacilli.**

*Harold W. Lyall, Am. Rev. Tuberc., 5:899, Jan., 1922.*

Uncertainty of successful results in the majority of methods proposed for direct isolation of tubercle bacilli from sputum and other fluids or excreta has led to a general feeling that the most reliable procedure is inoculation of animals, with subsequent isolation from the tissues at autopsy. Objections to this procedure are: (1) possible changes in virulence or growth characteristics in the organisms, and (2) the length of time before final isolation in pure culture. In the usual direct methods the manipulations involved favor the chance of contamination. The simplicity and reliability of the Griffith method (noted in 1914 and 1916) inspired the author to make the present investigation. Essentially the same technic was used: equal parts of sputum and 10% antiformin were mixed by shaking or stirring; a loopful of the mixture, after it had become partly liquified, was streaked directly onto suitable media. The best medium for the direct isolation of tubercle bacilli from sputum was one containing beef liver infusion and egg in the proportion of 1:4. The results were uniformly successful, tubercle bacilli being isolated in pure culture in 55 out of 56 specimens. Less than 5% of a large number of tubes showed any contamination. Except for a small number of cultures, a ten minute interval could be taken to yield pure cultures without contamination. The method is regarded by the author as a distinct advance.

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**Diagnosis of Tuberculosis Through Direct Inoculation of Artificial Media with the Sputum.**

*A. Calmette, Paris méd., 12:13, Jan. 7, 1922.*

When the microscopic examination of the sputum was negative, the only recourse, until recently, was to inoculate guinea-pigs with a specimen. This, however, is an expensive and slow method, as eight or ten weeks elapse before the results can be known. A new method has been devised by Petrof and Limousin which makes this unnecessary. It is based upon the use of media prepared with eggs and veal extracts, which are colored with gentian violet. The sputum is incubated for thirty minutes at 37° C. in a 4% sodium hydroxid solution, centrifugalized and made slightly acid. The egg medium is then inoculated with a few drops of the sputum. Tubercle colonies appear within eight to fourteen days. If 5 tubes have been inoculated, it will be found that at least 3 give pure colonies of tubercle bacilli. Very few other bacteria can grow, on account of the action of sodium hydroxid and gentian violet. This method has been used for several months with complete success by the writer. Every sample of sputum containing bacilli which was tested in this way gave cultures of tubercle bacilli.

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**Demonstration of Tuberculosis by a Short Method of Animal Experimentation.**

*Rudolph Oppenheimer, Deutsch. med. Wochenschr., 51:1557, Berlin, Dec., 22, 1921.*

The ordinary animal experiment requires six weeks, but if the material to be examined is injected into the liver of guinea-pigs the usual tuberculous changes and tubercle bacilli can be demonstrated after fourteen days. In the smooth brown fields of the liver fresh nodules are easily demonstrated. Injections are also made into the spleen, as the spleen becomes infected with tuberculosis easily. The technic is simple. As large amounts as possible of sediment are injected near organs which, like the spleen, are extremely susceptible to tuberculosis, or in which, as in the liver, tuberculous changes are very readily recognized.

(1d—148)

**Tularemia Francis 1921.**

*Edward Francis, Pub. Health Rep. (U. S. P. H. S.), 37:83, 96, 102, Jan. 20, 1921.*

**Transmission *Cimex Lectularius*.**—The common bed-bug transmitted tularemia from infected to healthy mice in 10 instances, in which the intervals elapsing between biting the infected and biting the healthy mice varied from a few seconds to seventy-one days. White mice that ate bugs infected as long before as 100 days usually contract tularemia. The fresh feces of bed-bugs which were infected with *Bacterium tularensis* by sucking the blood of infected white mice, and which were fed every ten days thereafter on the blood of healthy white mice, contained virulent organisms up

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to 120 days after the date of infection of the bugs. Tularensis suffered no apparent diminution of virulence by reason of residence as long as 120 days in bed-bugs.

*Transmission by Mouse Louse.*—The transmission of tularemia was effected in 12 of 17 attempts through the mouse louse (*Poly-pax serratus* [Burm.]) by the transfer of white lice from white mice dead of tularemia to healthy white mice. The urine of infected white mice was infective for guinea-pigs when injected subcutaneously but failed to infect white mice when fed to them. The mouse louse commonly found on the laboratory white mice was absent from 56 house mice caught in the laboratory.

*Cultivation of Bacterium Tularensis.*—The only culture mediums reported heretofore for the cultivation of *B. tularensis* are coagulated hen's egg yolk and hen's ovomucoid with a trace of yolk. The writer now reports cultivation of the organism on serum glucose agar, glucose blood agar, and blood agar, each of the foregoing mediums being used with a piece of fresh sterile rabbit spleen. The mediums were used for original isolation of this organism from animals, and the question of acquired adaptability to a new medium brought about by previous cultivation on a special medium is not involved. As growth on these mediums is scanty and of lowered virulence, coagulated egg yolk remains the best medium for routine isolation and cultivation of *B. tularensis*.

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Differential Centrifugalization. A Method for the Study of Filtrable Viruses, as Applied to Vaccinia.

*W. G. MacCallum and Ella Hutzler Oppenheimer, J. A. M. A., 78:410, Feb. 11, 1922.*

A viscid fluid containing 2.34% glycerin was used for this study. The specific gravity of this original lymph is 1.1638. The determinations of the specific gravity in all cases were made by weighing 1 c.c. of the fluid in a small and very narrow test-tube accurately calibrated to hold just 1 c.c. In such a test-tube the original lymph was centrifugalized at a high speed for an hour, and separated into a solid mass of sediment, a thick turbid layer and a superficial less turbid layer. The top layer was inoculated on the cornea of the right eye and the bottom layer on the left eye. In each case a typical vaccine lesion with ulceration appeared in the right eye, while the left remained unaffected. The top layer was transferred to another calibrated test-tube which was filled up to the mark with Locke's solution. After centrifugalization and inoculation as before, all the right eyes were unaffected and all the left eyes "took." In other words, the specific living infective agent was now found at the bottom of the tube. Its specific gravity therefore lies between 0.99 and 1.1638. A series of flasks were prepared with mixtures of glycerin and Locke's solution varying in specific gravity from 1.0 to 1.6, and with these suspending fluids the specific gravity of the virus itself was approached from both sides. Each mixture was weighed in the calibrated test-tube and the specific gravity of the final mixtures thus ascertained. After centrifugalization the top layer was inoculated into the right eye and the bottom

layers into the left. In this way it was found that the virus floats in a suspending fluid of specific gravity 1.14, while it sinks in a suspending fluid of specific gravity 1.11. Its own specific gravity is probably about 1.12 or 1.13. To purify it, therefore, it seems best to wash it and centrifugalize it in a suspending fluid just heavier than itself, for thereby a maximal removal of contaminating material will be attained. This method makes it possible to isolate and concentrate in suspension the infective agent of vaccinia, which can be contaminated only with other materials of the same specific gravity.

(1d—150)

Flagellated Intestinal Parasites of the Field Rat (*Microtus Arvalis Pallas*).<sup>(1d—150)</sup>

*G. Lavier, Bull. Soc. de path. exot., 14:710, Paris, Dec. 14, 1921.*

Parasites occurring in the blood of rats of this species have been described. Three forms of flagellated intestinal parasites have also been found in this animal, whose habitat is the region about Dijon: (1) Vegetative and cystic forms of Giardia. These correspond to the descriptions given by Kofoid and Christiansen. The author states that the parabasal bodies are elongated, pointed and slightly curved. Blepharoplasts were simple, never being found double. Between the 2 blepharoplasts there is a small chromatin granule, median, slightly anterior and connected with each blepharoplast by a thin chromatin filament. The average length of the nuclei is 2.2 microns, width 1.1 microns. The nucleus contains a long, lobulated karyosome. The species has not been finally determined. It is most similar to *Giardia intestinalis*, but the genus has not been fully studied. Some of the forms may be only variations of a single species. (2) Vegetative and cystic forms of *Octomitus muris*. (3) *Trichomonas muris* Hartmann.

(1d—151)

A Common Infusion Flagellate in the Cecal Contents of the Chicken.<sup>(1d—151)</sup>

*Cesar Uribe, J. Parasitol., 8:58, Dec., 1921.*

Uribe regularly encountered a small flagellate in cultures from material containing eggs of *Heterakis papillosa*, a parasite of the common fowl. It was also found in infusions contaminated with feces of the rabbit and in the cecal contents of young chickens which had been fed *Heterakis* material, so that it is evidently adapted to entozoic life. It is also found multiplying profusely in a variety of media outside the animal body. Certain species of the genus may occur as accidental parasites, retaining under such conditions the same characteristics as shown in their free state. Organisms similar to those described were found by Wight and Lucke in postmortem cultures and smears from various organs of soldiers who died from influenza in the 1919 epidemic. The writer studied the organism in fresh and stained preparations made from cultures at room temperature on "ameba agar". They grew most satisfactorily on this medium. The colorless, transparent, kidney-shaped organism, equipped with a flagellar apparatus, was observed during ingestion of food and multiplication by binary

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division. The classifications by Alexeieff and others are rejected in favor of placing the organism in the genus *Bodo*, Ehrenberg, until the structure described tentatively as a kinetonucleus is demonstrated as such, and also until the absence of kinetonucleus is established for the genus *Bodo* and its presence accepted as diagnostic of the genus *Prowazekia*.

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**The Wasserman Reaction and Coccidiosis of Rabbits.**

*Curt Marcuse, Cntrlbl. f. Bakteriol., etc., 87:355, Jena, Dec. 17, 1921.*

Kuśzinski expresses the opinion that the positive result of a Wassermann reaction in the case of rabbits which previously had not been treated, has some connection with coccidiosis, the most common disease of rabbits. He came to this conclusion because the presence of coccidiosis could be established each time when the Wassermann reaction was positive. Coccidiosis can be cured with mercury and salvarsan. Marcuse desired to control Kuszinski's claims. All animals used in these experiments were constantly examined as to the presence of coccidiosis (examination of excrements). Autopsy was made to control these results. The experiments of complement fixation were made according to the rules of the Wassermann reaction. These investigations show that, contrary to Kuszinski's claims, no connection could be established between the Wassermann reaction and coccidiosis. The results of the reaction fluctuated considerably in the case of normal rabbits. Animals affected by coccidiosis might react positively and healthy animals negatively, and vice versa. Complement fixation was not only made with Wassermann extracts, but also with alcoholic coccidiosis extracts, similarly to the complement fixation test in the case of echinococcus. For the preparation of coccidiosis extracts Marcuse used the liver of a rabbit which had died from a very malignant form of coccidiosis. No specific complement fixation could be obtained with coccidiosis extract. The Wassermann reaction was negative in the case of rabbits affected with genital spirochetosis. On account of these results it is advisable to be extremely careful when utilizing the indications of positive reactions of the serum of rabbits, as well as indications of their appearance and disappearance.

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**Coccidiosis of the Brown Rat (*Mus Decumanus Pall*) and Its Relation to Rabbit Coccidiosis.**

*Franz Rudovský, Cntrlbl. f. Bakteriol., etc., 87:427, Jena, Dec. 30, 1921.*

The author could not find coccidia in the liver or stomach of the experimental animals. Rat coccidia seem to be limited to the intestine. They are found throughout the year. At first sight the lymph-follicles, which are visible through the serosa and are of different sizes in different places, might be mistaken for foci of coccidia such as are found in advanced intestinal coccidiosis in rabbits. The author did not find such yellow foci in the intestinal wall in rats. The numerous coccidia were found only on microscopical examination.

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The examination of the feces is difficult; coccidia must be differentiated from flagellates and ameba cysts, *Eimeria falciformis* and *E. stiedae* and from *trichocephalus* eggs.

Thirty-five of the rats examined were infested with *Eimeria falciformis* and 4 with *E. stiedae*. The former were frequently found in young and apparently healthy rats; in older rats a few scattered specimens were found in the feces, on autopsy. The frequent appearance of *E. falciformis* in rats seems to be analogous to that of *E. stiedae* in young rabbits. It seems that rats, as well as rabbits, acquire increasing immunity with age. In the 35 rats infected with *E. falciformis*, sporulation was observed and the parasite was seen in cut sections. One case of a rat infected with *E. stiedae* was noteworthy because of the fact that a rabbit which had died of coccidiosis had been eaten by rats.

The author believes that the brown rat is the original host of the coccidia, and that they are transmitted to the rabbit. Transmission of rat coccidiosis to rabbits has been demonstrated in animal experiments. The oocysts of the eimeria have an extraordinarily resistant wall. This resistance was particularly apparent when the author observed the development of sporozoites in disinfectant solutions. The coccidia could not be destroyed by 2% creolin solution or 3% sulphuric acid, or 10% potassium bichromate. This shows how easily an animal might become infected in regions in which the presence of coccidia is not suspected or where they are supposed to have been killed. This fact should be taken into consideration in the disinfection of infected stables.

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**Studies on Microsporidia Parasites in Mosquitoes. II. On the Effect of the Parasites upon the Host Body.**

*R. Kudo, J. Parasitol., 8:70, Dec., 1921.*

While examining mosquitoes in Pennsylvania and New York last summer, Kudo found that the microsporidian infections of mosquitoes take a serious course, and that microspordia occur rather widely among different species of mosquito on this continent. He reviews the recorded occurrence of microspordia. A geographic distribution of microsporidia is given. Kudo's experiments on *Thelohania magna* in *Culex territans* and *T. illinoiensis* in *Anopheles quadrimaculatus* indicates that the infection often produces death in the larva. The rearing experiments on *Culex territans* indicates that infected mosquito larvae kept in captivity die in a much shorter time than uninfected ones. The pupas and adults which were examined were found to be free from the infection. During the course of the work on a collection of *Culex apicalis*, a new microsporidian infection was found. The writer proposes the name of *Thelohania opacita*. The most conspicuous symptom of the infection is a striking opacity of the body. No difference in size was detected between the healthy and infected larvae, but there was a marked decrease in activity. The morphology of *T. opacita* is described.

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Culture of Spirochaeta Icterohaemorrhagiae and of Spirochaeta Hebdomadis.

*Renjiro Kaneko, Cntrlbl. f. Bakteriol., etc., 87:345, Jena, Dec. 17, 1921.*

As the different writers cannot agree upon the vital conditions required for a successful culture of Weil's spirochetes and the spirochetes of seven-day fever, Kaneko tried to establish the most favorable conditions for such culture. It was found that human ascitic fluid was a very good liquid nutrient medium for the culture of these 2 species of spirochetes, particularly when some blood pigment was added.

Different species of spirochetes were cultivated on serums of different domestic animals and of human beings. Rabbit serum was found to give the best results. The spirochetes also grow well on mutton serum, less well on ass serum, and not at all on bovine and chicken serum. It is best to use the rabbit serum diluted with 2 to 5 parts of Ringer's solution. The presence of blood-corpuscles and of hemoglobin in the serum culture seems to have a favourable influence upon the growth. An addition of agar influences favourably the growth of the microorganisms in these liquid media. Agar in a concentration of 0.3% seems to be best for the growth of spirochetes. Temperatures below 35° C. may be considered the optimal zone for these spirochetes. An abundance of oxygen seems to interfere with the growth of the parasites. Slightly alkaline reaction of the medium gives good results. A heating of the medium up to 60° does not seem to have a great influence upon the growth. The growth of the spirochetes in the different culture media differs gradually according to the species. The degree of virulence seems to be of importance.

On the basis of these investigations the following methods can be especially recommended for the culture of the 2 mentioned species of spirochetes: (1) Liquid medium: a drop of rabbit blood is introduced into 2-3 c.c. of rabbit serum diluted with 2 to 5 parts of Ringer's solution. The mixture is heated at 56-58° C. for thirty minutes, and then covered with a layer of liquid, sterilized paraffin. (2) Semi-liquid medium; a mixture similar to the first (serum of other animals and ascitic fluid may also be used) is added to a 0.3% solution of ordinary agar. For this purpose 3 gm. agar are dissolved in 100 c.c. water. After heating as for (1), it is covered with a layer of liquid paraffin. The liquid substratum is well suited for current experiments in the laboratory, while the semiliquid product is particularly suited for producing large quantities of spirochetes for purposes of immunization, and also for prolonged conservation of cultures.

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Animal Experiments with the Spirochetes of Recurrent Fever.  
*G. Henning, Klin. Wechschr., 1:124, Berlin, Jan. 15, 1922.*

In a large number of white mice infected with recurrent fever there were 2 morphologic series of spirochetes. In one series they were always readily recognizable, did not become entangled, broke up into fragments that stained well, while in many specimens there were irregularities and interruptions in the black staining. Those of the

second series rolled up, became entangled and the knots broke down into irregular plump structures and irregular shaped bodies and fragments. The first series of forms, with a straight axis, were found in the veins and capillaries. The rolled-up forms were found in the very finest vessels of internal organs, especially the liver and spleen. The morphologic difference is possibly an expression of injury of varying rapidity.

There was no active extravasation of spirochetes from the blood into the tissues and cells; the spirochetes often wound around cells. The débris of broken down spirochetes was removed by phagocytosis. They became less as the intervals between attacks increased. During relapses the spirochetes appeared in greater numbers but not in such great numbers as at the height of the first attack; they were more varied in form and not all at the same stage of development. After salvarsan treatment there was a rapid decrease in the spirochetes, after six hours to a hundredth to a thousandth part; later they disappeared entirely from the blood. Compared with untreated animals, more delicate and unequally staining forms appeared more frequently, showed irregular staining and early breaking up into very small parts. Spirochetes and their débris were found for quite a long time in the liver capillaries. There is no neurotropism in the spirochete of recurrent fever. In the control nervous system there are signs of degeneration.

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**Study of Animal Parasites.**

*Leopold Karl Böhm, Cntrlbl. f. Bakteriol., etc., 87:407, Jena, Dec. 30, 1921.*

The author describes the cysticerci which he has observed. The cysts obtained from the host, in which the parasites floated free, are thin-walled and tolerably transparent, so that the contours of the cysticerci may be seen through them. They are generally egg-shaped or heart-shaped, and measure 2-5 mm. in their longest diameter. The larvae themselves are plerocercoids, in the sense in which the word is used by Braun: compact, flattened, pure white cysticerci without a caudal vesicle and without a tail, a little longer than broad, generally 1-2.5 mm., long with transverse folds and with a longitudinal fissure at each end of the body, the anterior of which is connected with the scolex invagination, the posterior with the excretory bladder. The invaginated scolex can be seen on the anterior end in the form of a milk-white, round disk. Uppermost on the body of the larva is a thin, structureless membrane; it corresponds to the hairy layer of cestodes. Beneath it is a broad layer which is homogeneous and stains bright red with eosin. Then there is a narrower layer which in sections seems to be made up of rods. After this layer, but separated from it by a narrow, clear zone, there are a series of cells arranged in palisades. These are the matrix cells of the cuticula or subcuticula. The body parenchyma fills the entire space which is not filled by the other organs, so that there is no hollow space corresponding to the mother vesicle of the cysticerci. Large numbers of calcium bodies are found in the head and neck parts, smaller numbers in the lateral parts, and in the posterior segment they are completely lacking.

Böhm takes up an argument against the nomenclature proposed by Braun, which he says is only provisional. As soon as the sexually mature forms are found, the species should be classified in the genus to which these sex forms belong. Genus names are an aid in description, insofar as they do away with the necessity for a great deal of description when the larva can be classified into large groups on the basis of certain distinguishing characteristics.

Braun divides the larval forms of cestodes into 4 groups: (1) cysticerci (larvas with a caudal vesicle; the coenurus and echinococcus belong to this class); (2) cysticeroide (with a caudal vesicle but without any contained fluid); (3) plerocerci (parenchymatous stages of development which contain no fluid); and (4) plerocercoids (forms which correspond to the plerocerci, that is, whose caudal part is entirely parenchymatous but is not separated from the head.)

Böhm believes that it is not possible to differentiate the last 2 classes. He thinks that the 2 names plerocercus and plerocercoid should not be used, but that all parenchymatous larvas, that is, cestode larvas without a hollow space in the tail, should be called plerocerci.

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**West African Ceratopogoninae.**

A. Ingram and J. W. S. Macfie, *Annals Trop. Med. & Parasitol.*, 25:313, Liverpool, Dec. 30, 1921.

This paper is a continuation of the series previously published on the ceratopogoninae of the Gold Coast and it contains descriptions of additional new species. Under genus Culicoides, Latr., detailed descriptions of either the measurements, structures or morphology of the male or female or of the pupa or larva are given for *C. austeni*, Carter, Ingram and Macfie; *C. distinctipennis*; *C. eriodendroni*, C., I. and M.; *C. grahami*, Aust.; *C. neavei*, Aust.; *C. similis*, C., I. and M.; *C. corsoni*, sp.; *C. inornatipennis*, C., I. and M., var. *rutilus*, var. nov. Under genus *Dasyhelea*, Kieff., either the pupa, larva, measurements of body, etc., head, male hypopygium or other structures are described for *D. fuscipleuris*, C., I. and M.; *D. nigricans*, C., I. and M.; *D. nigeriae*, sp. n.; *D. boothi*, sp. n.; *D. retorta*, sp. n. Comparatively the same structures are considered under the genus *Atrichopogon*, Kieff., for *A. africanum*, sp. nov.; *A. elektrophaeum*, sp. n.; *A. perfuscum*, sp. nov.; *A. chrysosphaerotum*, sp. nov.; *A. homoiom*, sp. nov.

The genus *Kempia*, Kieff., appears to be characterized chiefly by the presence of a well developed empodium on the legs and of the pubescence on the eyes, and of the absence of the longer hairs from the wings. The genus shows affinities to 3 different types of the Ceratopogoninae, the wing characters linking it with *A. trichopogon*, those of the eyes to *Dasyhelea*, and those of the early stages to *Forcipomyia*. The genus *Schizodactylus*, nov., is allied to *Xylocrypta*, Kieff., and *Xenohelea*, Kieff., but it is distinguished from *Sphaeromias*, Curtis, and *Palpomyia*, Mergele, by the characters of the fourth tarsal segments, which are cylindrical in both sexes, and by the antenna of the males, only the last 3 segments of which are elongated.

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**Three New Sheep Cestodes, and Data on Other Cestodes of Ruminants.**

*Rudolf Blei, Cntrlbl. f. Bakteriol., etc., 87:365, Jena, Dec. 17, 1921.*

The writer collected anaplocephalids from sheep imported from the Ukraine by way of Hungary. Morphologic examination showed some varieties which could not be identified with any of the known forms. The material was obtained in a way similar to the process of intestinal washing. Usually it was possible to classify cestodes macroscopically, in many cases even the species. Formalin was found best as a preservative.

After examining each specimen through a binocular microscope, the head, a short adjoining section, and a few sexually matured segments were stained with whole preparations of borax carmin. Sections were stained with Delafield's alum hematoxylin, iron hematoxylin (Heidenhain) and alum hematoxylin (Grennächer). The latter method gave the best and quickest results.

As a result of these investigations it is proposed to remove genera *Stilesia* and *Avitellina* from the subfamily of *Thysanosominae* and to create an entirely new subfamily, *Avitelliniae*.

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**Observations on *Chilomastix Intestinalis* Kuzinski.**

*Lamberto Leiva, J. Parasitol., 8:49, Dec., 1921.*

Since *Chilomastix intestinalis* was extensively found in the guinea-pig and is related to the human parasite, it is of general interest. *C. intestinalis* was detected in 11% of the guinea-pigs examined during the course of the investigation, excluding those animals which were artificially infected. The morphology of the free stages and the encysted stages was studied. The lumen of the intestinal tract from about 2 in. above the cecum posteriorly to the rectum was the site of infection. The infection is usually heaviest in the cecum. The trophozoites were found to be cecal, partly intestinal, and partly colonic, lumen-dwelling parasites. The cysts occurred at all levels but were more abundant posteriorly and in the fecal pellets. From a study of sections taken from the various portions of the gut, no evidence of tissue invasion was detected. The neuromotor system, including the parabasal body and axostyle, in *C. intestinalis* is similar to those described by Kofoid and Swezy for *C. davainei*. In the free form no division phase was seen, but cases of paramitotic fission were observed in a cyst. *C. intestinalis* of the guinea-pig is distinct from *C. davainei* of man; the differential characters are tabulated. The cysts of the former have a broader, less constricted anterior region and are stouter and somewhat wider. The external limb of the cytostomal rim of *C. intestinalis* has a deeper, more acutely pointed, lateral constriction than the more gently undulating one of *C. davainei*.

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Brazilian Helmithologic Fauna. Brazilian Species of the Family Gorgoderidas Loos. 1901.

*Lauro Travassos, Brazil med., 36:17, Rio de Janeiro, Jan. 14, 1922.*

The article lists the species of this family; with certain general descriptions of genera. Some of these parasites inhabit the urinary bladder of *Leptodactylus ocelatus*, some the gall-bladder of the salmon of the Plata and San Francisco Rivers; others belong to fishes of Asia and Australia. Their various measurements are tabulated.

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Phases in the Life History of a Holostome, *Cyathocotyle Orientalis*, Nov. Spec.

*Ernest Carroll Faust, J. Parasitol. 8:78, Dec., 1921.*

Description of *Tetracotyle orientalis* from Peking, China, is given. The excretory system of the holostome larvae consists of the bladder and the tubule system with the flame-cells at the termination of the capillaries. The system shows 5 main tubules on each side of the body, each tubule draining a system of 32 dorsal and 32 ventral capillaries and flame cells. Feeding experiments on young Chinese domestic ducks were undertaken to determine whether holostome larva could continue growth in this type of host. These ducks had never been near any ponds or canals, so were free from infections. One duck was infected with *T. orientalis* and died. Four ducks were infected with other larval trematodes. These ducks died after the other duck; autopsy showed no infection. The holostomes recovered belonged to the genus *Cyathocotyle* Mühling, 1896. Faust suggests the name *Cythocotyle orientalis* for this species. Comparison of tetracotyle, miniature and adult worm indicates changes involved in the growth of the parasite and relationship of the genus of the group.

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Study of Mermithides.

*G. Steiner, Cntrlbl. f. Bakteriol., etc., 87:451, Jena, Dec. 30, 1921.*

There has never been any workable classification of the forms of nematodes, chiefly because the greater number of nematode forms thus far described are not sufficiently well known. The author's studies were undertaken from a desire to test some of Linstow's species differentiations, which Steiner thinks were not well founded. The number of forms of mermithides will undoubtedly increase greatly in the future, and the tropics, with their great abundance of insects, which are the favorite hosts of these parasites, will undoubtedly furnish many of them. The author presents 2 forms from New Mecklenburg. The first form, *Mermis namatanaiensis*, is distinguished particularly by the extremely anterior position of the head papillas, the small beak-shaped lateral organs lying immediately back of the lateral papillas, the blunt, round tail of the female, and the 2 large powerfully developed ventral gland-cells. As to the second form found in New Mecklenburg, *Mermis nigrescens Dujardin var. athysanota*, Steiner calls attention to the fact that in the ova of this new variety the tasseled ap-

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pendage is completely lacking, as well as the circular ridge. The shells of the ova have an uneven, rough, almost warty surface.

The author discusses some types of the species of mermithedes described by Linstow. The first of these is *Mermis pusilla* (habitat, Lake Nyassa). The peculiar thickening of the body, and the position and form of the head papillas and lateral organs, are the chief characteristics of the species. As a second form he mentions *Mermis quadripartita* (habitat, Island of Reunion). Linstow described the peculiar distribution of the body fat, as seen in cross-sections, as the chief distinguishing characteristic of this form. But Steiner thinks that the species is not yet sufficiently known. He also criticizes *Mermis gracilis* (habitat Raupen in East Java), *Mermis truncatula Rudolphi*, *Mermis involuta* (habitat, Togo) and *Mermis pachyderma* (habitat, Buenos Aires). In *Mermis involuta*, Linstow seems to have seen only the submedian papillas, while, according to the author, there are 6 head papillas and 2 so-called mouth papillas. The latter are on the sides and further forward, near the mouth opening. In *Mermis pachyderma*, also, in which the head papillas lie further back, they are noteworthy. They are 6 in number. Linstow seems to have seen only the 4 submedian ones.

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**A New Human Trematode from Japan.**

*William W. Cort and Sadamu Yokogawa, J. Parasitol., 8:66, Dec., 1921.*

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In this paper is described a new human trematode of more than incidental occurrence, *Heterophyes nocens*, Oiji and Nishio, which was entirely unknown outside of Japan. Oiji found and reported on a peculiar type of trematode egg in a number of fecal examinations. *H. nocens* was found in the middle part of the intestines of man. Its eggs were found in 31 out of 168 fecal examinations made from the inhabitants of 2 Japanese villages. In the intestine the flukes were found between the villi and sometimes attached to the mucous membrane near the bases of the villi. A table shows the specific differences between *H. nocens* and the Egyptian species from man. The 2 species are distinct. The secondary host was found to be in fish, which are eaten raw by the villagers. This fact was substantiated by feeding experiments on laboratory animals. There is no evidence that the parasites break the intestinal mucosa, feed on blood or tissues or produce a toxin. Under a heavy infestation they might produce injurious results. These 2 species have a decided importance, since their eggs may be easily confused with those of *Metagonimus yokogawai*, Katsurada, an intestinal trematode of man in Japan, and with the human liver flukes of the genus *Clonorchis*. These latter forms are definitely pathogenic and their accurate diagnosis is difficult except by the discovery of their eggs in the feces.

**1e. IMMUNOLOGY, SEROLOGY AND HEMATOLOGY**

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**D'Herelle's Phenomenon.**

*IV. Rimpau, Münch. med. Wochenschr., 68:1649, Dec. 23, 1921.*

If a small quantity of feces is placed in nutritive bouillon and passed after a little while through a Berkefeld filter, the filtrate has the property of clearing up turbid solutions in nutritive bouillon of living bacteria (Flexner dysentery bacilli, for instance) after a few hours, by dissolving the bacteria. It requires only a very small quantity of the filtrate to do this. The lytic action is continued if small amounts of the clear dysentery bouillon is transferred to fresh turbid solutions. D'Herelle assumes that the process is caused by a living, ultravisible, filterable virus that penetrates the bacteria, increases, and is released again by the dissolution of the bacteria. This hypothetical microorganism he calls a bacteriophagus. Bordet brought about this phenomenon with the abdominal fluid of guinea-pigs that had been injected with colon bacilli, which justifies the conclusion that it is connected only with certain types of bacteria. According to d'Herelle, who isolated bacteriophages against typhoid, paratyphoid, plague and other bacilli, the normal habitat of the ultramicrobe is in the intestine, where it maintains itself at the expense of the colon bacillus. It adapts itself in its virulence to the individual bacteria, penetrates and destroys them. Epidemics die out when all susceptible individuals are infected with suitable bacteriophages. Bail and Gildemeister think that this active substance originates in the bacteria themselves and is not specific for a disease and that it is oftener specific for a certain strain of bacteria than for a species. Bordet's hypothesis that the substance originates in the bacteria is confirmed by Bail's observation that such active substances appear in the filtrates of old Flexner cultures. Gildemeister succeeded in producing the substance in test-tubes. The filtrates do not, as a rule, produce complete sterility of the bacterial solutions, but the bacteria which survive show changes in their growth. Bordet suspects that the lytic secretion arises from the bacteria when they have been affected by the leukocytes. Bail suggests the hypothesis that the bacteria are broken up into fragments by different influences but that these fragments preserve viability. They are filterable and in time break up other bacteria into fragments.

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**D'Herelle's Phenomenon.**

*R. Otto and H. Munter, Deutsch. med. Wochenschr., 47:1579, Berlin, Dec. 29, 1921.*

The phenomenon consists in the dissolving of dysentery bacilli in vitro by filtrates of the stools of patients sick with or convalescing from dysentery. The specific agent is tolerably resistant to heat and can be cultivated serially if traces of it are brought into contact with living dysentery bacilli in nutritive bouillon. D'Herelle thinks that the agent is an invisible bacteria-digesting microbe. He has used the "Bacteriophagum intestinale" with very good  
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results in the treatment of dysentery and other diseases. He found an effective therapeutic agent in the stools in 8 cases out of 14. He obtained the agent from cultures alone without infection of animals and without incubation with stool filtrates. With the bacteriophages obtained from bacterial cultures Otto and Munter developed 17 highly effective strains of virus against Shiga-Flexner and typhoid bacilli and against Shiga-Flexner and Y bacilli. They did not succeed in finding a lysin against colon bacilli. They confirmed d'Herelle's findings and succeeded in demonstrating the action of bacteriophages in animal experiments, but have not had any reliable therapeutic results in dysentery and typhoid in human beings. From the fact that the active agent was obtained from bacterial cultures and from other findings, the authors assume that d'Herelle's phenomenon is due to the action of a ferment contained in very fine fragments of bacteria.

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#### The Temperature Coefficient of Phagocytosis.

Wallace O. Fenn, *J. Gen. Physiol.*, 4:331, Jan. 20, 1922.

Previous workers (Madsen and Watabiki) have measured the effect of temperature on the phagocytosis of bacteria. In this article the author has reproduced the curves from the data of these authors, the ordinates showing the number of bacteria taken up per leukocyte as a function of time (abscissas) at different temperatures. In the curves the corresponding stages are not points of equal amount of action, because the maximum varies at different temperatures, but, rather, they are points of equal percentages of the total amount of action possible at that temperature. For comparative rates, therefore, one may take the number of bacteria ingested per leukocyte per minute during the first half of the reaction, i. e., until one-half the maximum number of bacteria has been ingested. The author believes that this criterion yields a value for the rate of the reaction which, though not ideal, is the best approximation possible under the circumstances. Following this procedure he calculated from the data of Madsen and Watabiki the rates of the reactions at different temperatures. In order to calculate from them the temperature coefficient,  $Q_{10}$  of the reaction the logarithms of these rates were plotted against the corresponding temperatures. The temperature coefficient for any interval of  $10^{\circ}$  on the abscissas is the antilog of the difference between the ordinates at the 2 temperatures, i. e., the slope of the graph for that interval. The resulting graphs were practically straight lines, which means that the temperature coefficient was constant over the entire range from  $5^{\circ}$  to  $35^{\circ}$  C. In other words, the rate of phagocytosis is very nearly a logarithmic function of the temperature from  $0^{\circ}$  to  $35^{\circ}$  C.; i. e.,  $Q_{10}$  is constant over that range and is equal to 2.

The author also reports new experiments as to the effect of temperature on the phagocytosis of quartz and carbon particles of uniform sizes, showing a marked increase in the temperature coefficient below  $30^{\circ}$  C. In each experiment a mixture of quartz particles 4.6 microns in diameter and carbon particles 4.7 microns

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in diameter was used. Then 0.3 c.c. of this mixture in distilled water was added to 1 c.c. of leukocyte suspension plus 0.4 c.c. serum plus 0.2 c.c. NaCl, 2.25%, plus 0.2 c.c. M/10 phosphate mixture of pH 7.5. Rates of phagocytosis, K, were taken equal to the reciprocal of the times, T, necessary for the ingestion of 25 per cent., 50 per cent., or 75 per cent. of the particles. T was determined graphically,  $Q_{10}$  was calculated by equation. The dispersion of the average was calculated where the data were adequate.

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**The Schick Test. Standardization of Diphtheria Toxin for the Test and of Heated Diphtheria Toxin for the Control; Methods of Diluting the Toxin.**

*Abraham Zingher, J. A. M. A., 78:490, Feb. 18, 1922.*

Standards for official control of Schick outfits are strongly advisable. The writer has found that  $\frac{1}{40}$  minimal lethal dose in 0.2 c.c. is the equivalent of the dilution recommended by Schick ( $\frac{1}{50}$  minimal lethal dose in 0.1 c.c.) in showing susceptibility or immunity to diphtheria. The larger amount of more diluted toxin is easier to inject, and the results are more likely to be accurate. The positive Schick reaction, also, in susceptible individuals who have not even a trace of antitoxin, is not likely to be so severe and to show the superficial necrosis of the skin noted with the more concentrated dilution recommended by Schick. To allow an official standardization and also an individual check on these outfits, it is suggested that no single outfit for the Schick test shall contain less than 1 minimal lethal dose of diphtheria toxin. Such outfits could be easily tested for potency in guinea-pigs, and would be sufficient for from 35 to 45 Schick tests. Outfits sufficient to make 5 or 10 tests cannot be tested for accuracy except in the human being. Undiluted bulk toxin accurately and carefully diluted is most suitable for the testing of large numbers of individuals, as in schools, institutions, hospitals, clinics. The dose of heated toxin for the control test has, in addition, a 20% excess, to allow for slight deterioration by heating of the reacting autolyzed protein. Emphasis must be laid on the accurate dilutions of the toxin for the Schick test and for the control test.

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**Serum Globulin in Kala-Azar.**

*Richard H. P. Sia and Hsien Wu, China M. J., 35:527, Shanghai, Nov., 1921.*

A study was made of Ray's so-called hemolytic test for kala-azar with the purpose of determining the nature of the turbidity and precipitate which forms when blood from a kala-azar patient is added to distilled water. Ray's assumption that the turbidity is due to incomplete hemolysis of the red blood-corpuscles, resulting from some change in the kala-azar blood plasma, was found to be incorrect. There was no difference observed between kala-azar serum and normal serum in their power to protect red blood-cells against hemolysis. It was found, however, that when kala-azar serum alone is mixed with distilled water a precipitate occurs.

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Chemical analysis showed the precipitate to be serum globulin. Quantitative studies of the globulin content of kala-azar blood revealed the fact that in this disease the serum globulin is not only much increased over normal but the concentration is higher than has been found in any other disease condition. This result is in keeping with the previous finding of the writers that the test was positive only in kala-azar. In view of these findings the writers suggest that Ray's hemolytic test be called the globulin precipitation test for kala-azar.

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**Studies on the Effects of Tuberculin.**

*Peter M. Holst, J. Hyg., 20:342, London, Dec., 1921.*

The problem of the effects of tuberculin in the organism in many respects is unsolved. Reference is made to researches of previous investigators. Holst performed a number of experiments to study the fate of tuberculin in the organism. A number of normal rabbits and guinea-pigs were injected intravenously and intraperitoneally. These experiments demonstrate that tuberculin rapidly disappears when injected intravenously or intraperitoneally into an organism. Franceschelli's conclusion, that tuberculin leaves the body through the kidneys and may be recognized in the urine some hours after the injection, was substantiated. Other experiments proved that in the meantime the tuberculin is bound in the organism, probably in the bones and in the liver. A large number of complement-binding experiments were undertaken with no desire to determine the quantity of complement-binding antibodies in tuberculin serums, but to investigate the nature of the alexin in these serums, and the nature of its combinations with antigens and antibodies. Holst deviated from the usual complement fixation tests. He divides these experiments with human serums into 2 groups: (1) those with complement derived from persons whose relation to tuberculosis was unknown, (2) those with complement derived from tuberculous persons. Of (1) there were 182 serums examined and 12 of these gave a different reaction to the others. Of (2) 35 serums were examined. These were compared with 296 serums from other persons, the majority of which were mentioned under (1). These experiments show (a) that the complements of different serums not infrequently show differences; (b) that differences may also be found between complements derived from individuals of one species; (c) that probably the complement of a tuberculous individual differs from that of the healthy subject.

The object of the experiments with phagocytosis was to determine whether tuberculin had any toxic effects upon the leukocytes, and whether it affects the leukocytes from healthy organisms in the same way as it affects those from an organism suffering from tuberculosis. The method of the emigration or chemotactic tubes of Wright was used in the study. The results showed clearly that tuberculin had a distinct and characteristic inhibitory effect upon the motility of leukocytes, therefore an inhibitory influence upon the phagocytosis. Other experiments proved that

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tuberculin was more toxic to corpuscles from tuberculous organisms than from nontuberculous organisms. A certain protective power in regard to the toxic action of tuberculin is found in the serum. This power is greater in serum from normal organisms, than in serum from tuberculous organisms. The difference of the effect of tuberculin upon normal and tuberculous leukocytes was demonstrated by vital staining, Manson's and other stains being used. The phenomenon of anaphylaxis in connection with tuberculin is considered at length.

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**The Aqueous Extract of the Tubercl Bacillus.**

*Fernand Berlioz, Bull. Acad. de med., 87:23, Paris, Jan., 3, 1922.*

The method of preparation is as follows: The bacilli are killed at a temperature of 110° C. and pressed between sheets of blotting-paper to remove the glycerin. They are mixed with 1.5 times their weight of carborundum powder and ground in an agate mortar. The mixture is digested in distilled water and incubated at 40° C. for three days, filtered and evaporated at 40° C., until there is no longer a loss of weight. A brownish-yellow sirupy liquid is thus obtained, which is thought by Berlioz to represent approximately the protoplasm of the bacilli freed from their cuticle, and is therefore called "protobacilline".

A single dose of 0.6 gm. has no effect on a guinea-pig. Doses of 0.1-0.2 gm., repeated during twenty days, kill the animal within forty-five days, without loss of weight. Injections of 0.6 gm. and 0.05-0.10 gm., repeated every three or four days for several weeks, are harmless when they are administered to tuberculous guinea-pigs. Protobacilline does not give rise to Koch's phenomenon. Several guinea-pigs were vaccinated with protobacilline before being infected with tuberculosis, others were treated in this manner both before and after the infection, and in still another group treatment was begun on the seventh or tenth day of the infection. Some of the treated or vaccinated animals survived somewhat longer than the control guinea-pigs. It is noted that the treated animals had very few tubercles, but rather showed lardaceous patches where histologic examination did not reveal the presence of any tubercle or caseation.

Only patients in the last stages of tuberculosis were experimented on, so that the influence of protobacilline on the course of the latter could not really be ascertained. The temperature, however, was decreased, and this effect persisted for several days. The injection was not followed by any local or general reaction.

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**The Serologic Test in Typhus.**

*W. James Wilson, Lancet, 1:222, London, Feb. 4, 1922.*

If bacilli from 18 hours old broth or agar cultures are suspended in a small volume of saline and rapidly dried at 37° C. in vacuo, they readily form a uniform emulsion when saline is added, after which more rapid agglutination occurs than even with living cultures. Moreover, in the dried condition, the agglutin-  
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ability appears to be retained indefinitely, either at room temperature or in the incubator at 37° C.—at least, the writer has found these dried cultures as sensitive after nine months as at the beginning of the experiment. After desiccation, on being suspended in salt solution, the emulsion can be preserved for some weeks in an active state by the addition of 1:1000 formalin. This does not affect the sensitiveness to typhus serum agglutinins, although with undried cultures it has this effect. The drying of bacilli renders them much less agglutinable by specific agglutinins. This is the case with *Bacillus typhosus*, *paratyphosus A* and *B*, and *Bacillus coli*. *Proteus X 19* forms no exception to this rule. It would seem that the typhus serum agglutinins for *X 19* are different from those produced in the blood of an animal by inoculation. Coliform nonlactose fermenting bacilli are occasionally found in typhus urine and are agglutinated by the serums not only of the individual patient but of other patients. On one occasion a strain of *Bacillus pyocyanus* was isolated which was agglutinated by a few of the typhus serums.

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**The Production of X 19 Agglutinins in Rabbits Following Infection with Rabbit Typhus Virus.**

*E. Weil and Th. Gruschka, Ztschr. f. Immunitätsf. u. exper. Ther., 33:207, Jena, Dec. 7, 1921.*

The constant appearance of *X 19* agglutinins in rabbits infected with typhus, and the fact that guinea-pigs infected with the virus of typhus are protected against a virulent culture of *X 19*, demonstrate that typhus agglutination in man is caused by the typhus virus, and that specific antibodies for *X 19* are produced.

Tests were carried out to determine the agglutinogenic power of rabbit virus when passed to rabbits. These tests have shown that the brain of rabbits infected with typhus virus produces in rabbits agglutinins for *X 19*. However, they are diminished qualitatively; the titer is lower than when the rabbits have been infected with the brain of infected guinea-pigs. Together with the H form of *X 19*, the O form was always used; the latter yields more uniform results and is not sensitive to variations in medium.

Neither guinea-pigs nor rabbits react with the production of agglutinins to the inoculation of  $\frac{1}{1000}$  of a loop. The agglutinin titer depends upon the amount of antigen and the species of animal used for its production. This was demonstrated in experiments with rabbits and guinea-pigs.

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**The Reliability of the Wassermann Test as Performed by Different Pathologists.**

*Joseph W. Bigger, J. Hyg., 20:383, London, Dec., 1921.*

The object of the work which Bigger records was to discover in how far the results of the Wassermann tests, performed by 5 pathologists working under the various Venereal Diseases Treatment Schemes of the Local Government Board in Ireland, agreed with one another. Samples of blood were obtained from 30 male

patients. All treated cases had received injections of novarsenobillon intravenously and, in the majority of the cases, mercury cream intramuscularly. Bigger divided each serum into 5 parts, and sent 4 batches of serums to the pathologists, who knew nothing about the serums in question. Pathologist A used the method described by Harrison. B used Harrison's method, except that the antigen was one prepared by Burrough, Wellcome and Co.; he recorded his results in the same way as A. C used Harrison's method slightly modified. A bullock heart extract containing 0.4% cholesterol was used for antigen. D used the "one tube" method of McIntosh and Fildes. E used a 2 tube method, 2 antigens being used. The results were recorded in the same way as D. Tables show the results of all the tests. There was a considerable degree of uniformity of results. The differences were chiefly in the case of weakly positive serums. The main source of the differences lies in the use of different methods, and not in any lack of personal ability or care in the case of the pathologists. If a uniform method of performing the test was adopted and the details of the method standardized, a number of these differences could be greatly reduced.

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**The Relation between Organic Decomposition Products and the Wassermann Reaction.**

*W. Bachmann, Ztschr. f. Immunitätsf. u. exper. Ther., 33:233, Jena, Dec. 7, 1921.*

Wassermann's doctrine as to the lipoid antibody is taken by Much as a proof of the correctness of the conception of lipoid and fat antibodies introduced by Much into the theory and practice of tuberculosis immunity. Experiments conducted by Mahlo at Much's laboratory aimed at proving the phenomenon that negative human serum, as well as the serum of treated immunized rabbits, become positive in the test-tube following the addition of amino-acid, and that, on the other hand, positive rabbit serum becomes negative under the influence of injected amino-acids as long as the latter can be demonstrated in the animal organism.

Mahlo proceeds from the assumption that organic decomposition products in definite amounts cause the positive Wassermann reaction in luetic serum, and attempts to prove, by means of the ninhydrin reactions, the presence of abiuretic albumin split-products in luetic serum. He compares the result of the ninhydrin reaction of such serums with that of the Wassermann reaction, and concludes that luetic serums freed from albumin give corresponding results (positive Wassermann reaction and positive ninhydrin reaction) in 79% of the cases. Much and Schmidt conclude that a pure amino-acid, as well as a pure lipoid, is able to convert a previously negative reaction into a positive one in the animal body, and that an indirect action via the body cells is to be assumed, since this effect of amino-acids upon the reaction does not occur in the test-tube experiment. These experiments have been repeated by the author.

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To begin with, the influence of glycocoll, trypsin, leucin and dimethyl-urea on Wassermann-negative human inactivated serum was tested in vitro, and it was found that the addition of glycocoll and leucin rendered previously negative serum positive. With glycocoll this was sometimes parallel to the concentration of the glycocoll solution added. In another series of tests the influence of the parenteral ingestion of amino-acids upon the result of the Wassermann reaction in rabbit serum was determined. It was possible to influence the result of the Wassermann reaction in rabbit serum by the injection of amino-acids (glycocoll, leucin) as well as of partial antigens. The interpretation of these results calls for great caution, since marked fluctuations occur in the serum of rabbits not so treated. In a direct series of experiments, Wassermann-positive and Wassermann-negative serums, as well as inactivated human serum which had been freed from albumin, were tested with ninhydrin reaction. The serums were tested for complete removal of albumin by the biuret reaction, with sulphosalicylic acid and with Spiegler's reagent. They were required to be as clear as water. To 2 c.c. of this filtrate were added 0.2 c.c. of a 1% solution of ninhydrin, and the mixture was boiled one minute. A violet color indicated a positive reaction. The results of the ninhydrin reaction in dealbuminized syphilitic serum accorded well with those of the Wassermann reaction. It is possible that the reaction depends upon steps in the decomposition of organic cells, but nothing can be stated as to its nature.

It has not yet been conclusively proven that the Wassermann substance is a lipoid antibody and that the Wassermann test is an antigen-antibody reaction.

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**Variations in the Complement Content in Guinea-Pigs.**

*Walter Loew, Wien. klin. Wchschr., 35:12, Jan. 6, 1921.*

The writer observed, in Siberia, that the Wassermann reaction was more frequently negative in summer than in winter. It was found that this difference was always due to variations in the complement content of the guinea-pig serum. The complement content was highest in summer (1:35), dropped in autumn to 1:15, remained stationary throughout the winter at from 1:15 to 1:20, and dropped again in early spring to 1:10. In Europe such pronounced variations do not seem to occur. No human material was investigated in Siberia. But Loew noticed that severe epidemics occurred just at the time at which the complement content was lowest (in September and in early spring).

The writer eliminated these disagreeable variations by titrating the complement of the inactive serum with which he worked, and using for the main experiment a comparatively slight but always proportionate excess of complement. Further he worked with the quadruple titer of the ordinary dissolving doses of hemolysin. With this method Wassermann reaction gave the same results in summer as in winter. Further, the number of complete inhibitions increased in comparison with partial ones.

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The Rational Preparation of a Hemolytic Amboceptor of High Potency.

*G. Kabrhel and M. Kretba, Casop. lék. česk., 61:21, Prague, Jan. 14, 1921.*

It is very important to have a good amboceptor serum for the successful execution of a Wassermann reaction; the best results are obtained by the use of guinea-pig complement, 0.05 c.c. of which has a hemolytic titer of 0.001-0.0005 c.c.

Wassermann's instructions for a successful preparation of a good amboceptor serum do not always lead to the desired results. Usually it is impossible to reach the desired titers. If the prescribed injection is repeated, the animal develops symptoms of anaphylaxis and usually dies. The writer investigated the problem as to the possibility of eliminating hazard by working methodically, and of thus obtaining a hemolytic amboceptor of high potency by following certain definite rules, and at the same time avoiding anaphylaxis. Kabrhel was guided in his experiments by the well-known fact that a group of muscles which was developed through exercise to a certain power, but had lost this power through an interruption of the exercises, can regain the same power through less exercise than was necessary to attain the same strength originally. If to the small dose which is required to reattain the same degree of strength a certain surplus is added, a higher degree of strength must necessarily be obtained.

It was assumed that similar conditions prevailed in the formation of antibodies—although this assumption is not in accordance with the usual practice, as larger doses are administered successively in order to attain a high degree of immunity—and the experiments were arranged accordingly. It was found that this assumption was correct in the case of precipitin, agglutinin and partly in the case of hemolysin. It is certainly very interesting to find an analogy in the functions of such widely different parts as musculature, brain and the organs producing antibodies.

For the experiments the following facts were also taken into account: the lower the hemolytic power of the blood, the less is the danger of anaphylaxis. Before making a second injection, it was therefore necessary to determine the decrease of hemolysin in the blood. As in the case of reinjection the conditions for the formation of hemolysin are more favorable, it does not seem necessary to begin immunization with a large dose. Therefore, the following rules were adhered to: (1) The same dose was used for all injections; (2) the injections were made with 0.5 c.c. of a 5% emulsion of sheep's erythrocytes; (3) after each injection there was a prolonged interval of rest. In this way amboceptor serum of very high hemolytic titer was obtained, and the symptoms of anaphylaxis either did not appear at all, or were very slight. The results are compiled in a chart.

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**The Thermostability of Fixed Antibodies (Studies in Hemolysin. I.).**

*Fritz v. Gutfeld, Ztschr. f. Immunitätsf. u. exper. Ther., 33:198, Jena, Dec., 7, 1921.*

Experiments were conducted to clear up the question of the heat resistance of reacting substances, in corroboration of Friedländer's claim that immune bodies fixed to their antigen are thermostable. Organic cells (sheep's blood), as well as organ antiserum, were tested under different thermic conditions. At 120° C. the fixing function of horse kidney and sheep's blood remained unaltered; at 160° C. it was diminished, and at 200° C. it was destroyed. Tests made with antiserum showed that heating to 62° C. for fifteen minutes had no effect; at 65° C. the hemolytic function was weakened, and it was destroyed at 70° C.

Tests to determine the thermostability of organ antiserum fixed to its antigen were carried out as follows: An emulsion of sheep cells was laden with organic antiserum to complete saturation. After washing and repeated centrifugation, the saturated cell emulsion was heated and antiserum was again added. If this combined with the sheep cells, the first antibody remained intact and fixed, despite heating. A second tube containing the same amounts of cell emulsion and amboceptor, but unheated, was used for control. The thermostability of the heterogenetic amboceptor (organic antiserum) fixed to fresh sheep erythrocytes, as well as that fixed to organic extracts, was tested. In the fixed state heterogenetic amboceptor was destroyed by heating, exactly as in the free state. This was proven: (1) by the fact that saturated organic antigen was again rendered free to fix amboceptor when the mixture was heated; (2) by the transgression test, which, after heating, was negative. Nothing has thus far been found to decide the question whether or not the cytophilic group of the amboceptor is destroyed by heating. The effect of heat upon the fixed amboceptor certainly consists in the destruction of its complementophilic and probably also of its cytophilic group.

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**The Relations of Bang and Forssman's Lipoid-Resembling Hemolysinogen to Heterogenetic Sheep-Blood Hemolysins. The Antigen Nature of Lipoids.**

*Hans Schmidt, Ztschr. f. Immunitätsf. u. exper. Ther., 33:216, Jena, Dec. 7, 1921.*

The injection of sheep erythrocytes into rabbits causes the production of antibodies capable of dissolving not only sheep erythrocytes but also those of beef. Such antibodies, produced by sheep blood-cells and directed against them, are known as isogenetic antibodies. These isogenetic sheep-blood antibodies are completely bound in vitro by sheep erythrocytes, but only partially by beef and goat erythrocytes. The injection of emulsions made of the organs of guinea-pig, dog, cat or horse, produces in the rabbit hemolytic antibodies for sheep erythrocytes, which are designated as heterogenetic. Sheep erythrocytes possess 2 antigens, one of

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which causes the production of the isogenetic antibody, while the other occurs in the cells in small amounts only, but is thermostable and can, therefore, be obtained pure from a boiled suspension of erythrocytes. This thermostable antigen also occurs in the organs of the above animals, and is known as heterophilic antigen, since it produces heterogenetic antibodies. It does not occur in the organs of human beings, or in those of sheep, rabbits, rats, cattle, pigs, pigeons, geese or frogs. Nearly all the organs in the guinea-pig group (lung, kidney, heart, but not blood and fat) contain the heterophilic antigen, which can be extracted with alcohol and produces a specific flocculation with sheep-blood, rabbit-immune serum, due to the presence of a heterogenetic antibody. The flocculation depends upon the presence of lipoids; the heterophilic antigen is probably a lipoid in the alchololic solution.

Bang and Forssman have isolated from beef serum a lipoid-like body which produced in rabbits a high titer ox-blood hemolysin. An attempt was made to obtain from sheep's blood cells a similar lysinogenic body which, probably, would constitute the heterophilic portion of the blood-cell antigen, and would probably also be of a lipoid nature. An immune serum produced in rabbits with the lipoid antigen from sheep blood-cells would be of the pure heterogenetic type. Such immunization experiments were carried out with rabbits. For preliminary treatment the animals were injected with substances from organic cells of the guinea-pig group and with substances from sheep blood-cells. With the latter test 3 rabbits were injected with the acetone-soluble portion of the blood-cells freed from fat and lipoids as far as possible, and with sheep blood-platelets, respectively. These serums were used in hemolytic experiments with sheep blood-cells, in flocculation tests with dog's lung, in complement-fixation tests with sheep blood-cells (after inactivating the serum) and in hemolytic tests after fixation, and in hemolytic tests following fixation and flocculation. A critical review of the results obtained appears to show that Bang and Forssman's lysinogen from sheep blood-cells is not a pure heterophilic antigen. The serum obtained with it from rabbits does contain some heterogenetic lysins, but the bulk of the lysins are serologically different from both heterogenetic and isogenetic antigens.

The serum obtained with blood-cells freed from fat, on the other hand, contains no heterogenetic antigens at all, but a small amount of isogenetic antigens. Hence the lipoid resembling lysogenic principle of sheep blood-cells corresponds only in part to the antigen of the guinea-pig group. The serum obtained by injecting rabbits with sheep blood-platelets is a purely isogenetic sheep-blood immune serum.

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The Influence of Temperature on Hemolysis through Hypotonia.

Adolf Jarisch, *Pflüger's Arch. f. d. ges. Physiol.*, 192:255, Berlin, Nov. 12, 1921.

Jarisch investigated the concentrations of common salt solutions which are necessary for maximal hemolysis at various temperatures with respect to the blood-corpuscles of man and several species of animals. At higher temperatures, a lower concentration of the salt solution is required; in other words, the resistance of the erythrocytes is greater. The resistance of the red blood-corpuscles is a function of temperature; it increases from 0° C. to a maximum at 45-50° C., after which it rapidly decreases, because these higher temperatures having themselves a hemolytic effect. The various animals react differently; the order of increasing susceptibility is as follows: sheep, ox, dog, man, rabbit, guinea-pig, horse. In correspondence with the variable quantity of phosphorus contained in the erythrocytes, it was found that the influence of temperature on the erythrocytes of the ox is increased by the addition of phosphates. Sodium sulphate and sodium tartrate had no effect. A mere inhibition of turgescence is therefore out of question; but the effect of the phosphates must be attributed to the modification of the distribution of ions. Buffer-mixtures of phosphates keep the concentration of hydrogen ions constant; therefore, as temperature rises, the concentration of hydroxyl ions must increase in proportion to the increased dissociation of the water; the hydroxyl ions combine with the protoplasmic colloids and increase the resistance exactly as fixed alkali does. If, vice versa, the hydroxyl ions are kept constant and the hydrogen ions are increased, which can be done by mixtures of ammonium, this is found to result in a corresponding decrease in the influence of temperature.

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The Agglutinopoietic Action of Normal Serum in its Relation to Hemagglutination and Hemolysis.

Otto Olsen, *Ztschr. f. Immunitätsf. u. exper. Ther.*, 33:238, Jena, Dec. 7, 1921.

Precipitation of normal serum with CO<sub>2</sub> generally enhances agglutination; this finds expression in an increased agglutination titer. Apparently, it is the same action of the complement and the CO<sub>2</sub> sediment which is known in bacterial agglutination, and which, possibly, is produced by the same precipitation-increasing action of the globulin fraction which Gengou has described. This agglutinopoietic action of the CO<sub>2</sub> sediment of normal serum results not only from the use of immune serum, but also occurs with normal serum containing normal agglutinins for homologous or heterologous erythrocytes or the red blood-cells of the same animal, upon the addition of immune serum or of such normal serums as are characterized by their high content of normal agglutinins.

Experiments were carried out to obtain information as to the characteristics of the factors producing the reaction, as well as

concerning the relation between hemagglutination and hemolysis. It was necessary to determine whether or not the characteristics of the agglutinopoietic agent agreed with those of the mid-piece, the end-piece and the third component, which are the 3 known fractions of complement. The agglutinopoietic agent was found in the sediment after precipitation with  $\text{CO}_2$ . No such properties were found in the filtrate which contained the end-piece of complement. If we designate as mid-piece those constituents of the sediment of guinea-pig serum resulting from  $\text{CO}_2$  precipitation or dialysis, the third component will be that fraction of the mid-piece which partly remains in the albumin fraction, and partly passes over into the globulin fraction, with acid precipitation of guinea-pig serum. In tests with agglutination or hemolysis the agglutinopoietic factor was still more resistant to heat than was the relatively thermostable third component. After heating to  $56^\circ \text{ C}$ . for half an hour, the agglutinopoietic action of the globulin fraction was unchanged, and it remained uninfluenced by Brand's modification of the mid-piece.

The tests have proven that normal serum, to which has been added immune serum or normal serum rich in normal agglutinins, increases the agglutination of homologous and heterologous erythrocytes, as well as those of the same animal. This action is bound to the precipitate obtained with  $\text{CO}_2$ ; it is absent from the supernatant fluid, but it differs in important particulars from the action of the entire mid-piece and the third component. Probably, it is exercised by a special portion of the mid-piece.

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**Immunologic Reactions of Bence-Jones Proteins. I. Differences between Bence-Jones Proteins and Human Serum Proteins.**

*S. Bayne-Jones and D. W. Wilson, Bull. Johns Hopkins Hosp., 33:37, Feb., 1922.*

This study of the nature of the "Bence-Jones proteins" found in the urine of patients suffering from multiple myelomas, is based upon the author's possession of a specimen of Bence-Jones protein which has the property of spontaneous crystallization. It could therefore be used for various immunologic tests, because it was purifiable. It was found to have specific immune reactions, as demonstrated by the use of precipitin reactions, the test of absorption of antibodies, complement fixation, and the production of anaphylactic sensitivity. Other Bence-Jones proteins, noncrystalline, and isolated from the urine by various salting out and other precipitation methods, proved not to possess such high specificity, but on the contrary gave reactions indicating that they contain traces of human serum proteins. The conclusions are that a good deal of previous immunologic study of the Bence-Jones proteins has been vitiated by lack of purity of the specimens used as antigens; that Bence-Jones proteins are immunologically different from normal human serum proteins; and that these differences between proteins from the same animal support the concept that chemical constitution, and not biologic origin, determines the specificity of proteins.

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**Interferometric Analysis of Immunity Precipitation.**

*R. Doerr and W. Berger, Biochem. Ztschr., 123:144, Berlin, Oct. 25, 1921.*

Doerr has demonstrated in a previous communication that interferometric analysis of immunity precipitation showed the same proportions as the flocculation produced in albuminous solutions by salts of thorium and cerium. In connection with these problems of interpretation of the most important immunity reactions (precipitation, anaphylaxis, agglutination), the writer undertook further experiments in order to establish what kind of conclusions could be drawn from changes in refraction concerning the nature of a chemofermentative process, and also what influence immunity precipitation had upon refraction. It was found that the phenomena of refraction were the same in the case of immunity precipitation as in that of flocculation of albumin by inorganic colloids, and further that no change in refraction occurred during the first phase of precipitation, which lasts from the moment of adding the precipitating agent to the body to be precipitated and from the beginning of flocculation. Loew's interferometer for solutions was used for these investigations. A long line of experiments were made in order to establish the phenomena which occur when mixing liquids which do not react with one another, and also when mixing liquids which do react with one another; further, the phenomena in reactions of fermentation, also in the mixing of albuminous solutions (serum) with bases and acids, and lastly in the case of chemo-colloid flocculation. In the case of immunity precipitation, the writer made indirect refractometric determinations of the precipitated mixture of antigenic antibodies, and undertook direct interferometric observations of immunity precipitation. It was found that an almost absolute conformity existed between the results obtained by the direct and by the modified indirect methods, as far as such conformity is practically possible at all. The refraction of the mixture of precipitating agent and the body to be precipitated showed a value which could be expected if no chemicomolecular transposition took place. An increase in refraction was never observed with progressing time of reaction. As the reaction between albuminous and immunity serum does not change the reaction during the initial period which lasts until the beginning of flocculation interferometric examination does not support the hypothetical interpretation of immunity precipitation as a reaction of protective fermentation.

The refractometric method does not supply any facts which would indicate the existence of decomposition. Consequently it is impossible to uphold the hypothesis concerning the fermentative decomposition of albuminous antigens by their antibodies.

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**Study of Spontaneous Agglutination in the Colon-Typhoid Group of Bacilli.**

*O. Ishii, J. Bacteriol., 7:71, Jan., 1922.*

In plating stock cultures upon 2% agar plates, 2 distinct types of colonies were found. The first presented a smooth surface and a regular outline and was not spontaneously agglutinated. The second showed a heavier growth, had a rough surface and irregular outline, and was spontaneously agglutinated. Spontaneous agglutination of a number of the members of this group was observed in peptone water, glycerol broth and glucose broth. In broth cultures, when flocculi are visible, macroscopic observation may be relied upon; but in cloudy cultures, microscopic examination should always be employed. Spontaneously agglutinated organisms are longer and are more motile than those which are not spontaneously agglutinated. Observations were made on colony changes in artificial culture media. Broth cultures of the isolated colony were kept at 37° C., and transplanted every second day, then examined for any change of colonies by streaking on agar plates. It was found that colonies of many strains of the colon-typhoid group may lose the property of spontaneous agglutination, while others that do not show this property at first may show it after some time. The period at which the change in colony occurs depends upon the strains; some strains always change within a short time and others only after many days. In isolation of types of colonies from stock cultures, 3 types were found: pure colonies, not showing spontaneous agglutination, those showing spontaneous agglutination, and mixed colonies showing the presence of both types. When run through animals and then plated, most of the colonies were of the nonspontaneously agglutinating type, but when subcultured developed both types. Every member of the colon-typhoid group was found to be changeable and may develop the 2 types of colonies, dependent upon duration of cultivation or other circumstances of growth, as well as upon the type of artificial culture medium employed.

Spontaneous agglutination occurs in a greater or less degree in glycerol broth, peptone water and all acid media, as is indicated by the results of experiments, but alkaline media inhibits spontaneous agglutination. In some growth tests, the nonspontaneously agglutinated bacilli daily exceeded that of the spontaneously agglutinated bacilli; in others, vice versa; in still others a parallel growth was observed for both. In experiments on specific agglutination with different types of colonies, no difference was found in the power of agglutination with 2 types of colonies of one strain.

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**Studies upon Agglutination in the Colon-Typhoid Group of Bacilli.**

*O. Ishii, J. Bacteriol., 7:39, Jan., 1922.*

Ishii reports the action of formalin, acid, alkali, and salt. on the agglutination power of the colon-typhoid group. A concentra-

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tion of 0.05 to 0.2% formalin prevents spontaneous agglutination almost entirely in some instances and entirely in others with *Bacillus typhosus*, *B. paratyphosus A* and, in a lesser degree, with *B. paratyphosus B*; formalin had no effect on the agglutinability of *B. coli*. Tables show the effect of formalin in various dilutions on the various bacteria. While formalin prevents spontaneous agglutination, it increases specific agglutination. Ishii used the following technic in his experiments: eighteen to twenty-four hour cultures in neutral broth at 37° C., were used as an indicator of spontaneous and nonspontaneous agglutination; 0.3 c.c. of each suspension of bacterial cultures in each medium is mixed with 0.3 c.c. of the serum dilution with formalin or without, or with other experimental fluids in small tubes, of the usual Wassermann type. The tubes were left at room temperature and the preparations were examined macroscopically and microscopically.

The action of formalin on pseudo-agglutination in the cross agglutination reaction with different immune serums prevents agglutination to a large extent. Normal horse serum was found to agglutinate almost every strain of *B. dysenteriae* and *B. coli*. These results confirmed the findings of previous investigators. Cultures in acid medium in which there is heavy growth and active motility yield stronger agglutination than cultures in neutral broth with *B. typhosus* and *B. paratyphosus A*; this effect is less noticeable in cultures of *B. paratyphosus B*, *B. dysenteriae* and *B. coli*; but the agglutinating power of these organisms is very weak in alkaline media; therefore the use of alkaline media is not favorable for agglutination tests. There is slightly less tendency to spontaneous agglutination in a broth medium than in salt solution. Tests showed no difference in the degree of agglutination reaction when using strong or weak solutions of sodium chlorid; only traces are necessary for agglutination. Glucose broth cultures of *B. paratyphosus A* and *B* and *B. coli* showed a tendency to spontaneous agglutination; *B. typhosus* showed weaker specific agglutination in glucose broth, but stronger in peptone water, only occasionally showing spontaneous agglutination. The dysentery group showed weaker agglutination with glucose broth cultures than with plain broth, peptone water and agar cultures. Peptone water cultures in general show a slight tendency to spontaneous agglutination, when nonspontaneous agglutinating bacilli are grown therein. This is difficult to prevent even when formalin is used. Agar cultures showed much weaker agglutination than broth and peptone water cultures. All the cultures were grown at 37° C. for twenty-four hours in neutral broth, 1% glucose broth, 1% peptone water, and on agar, the agar cultures being emulsified with salt solution. The cultures grown in plain broth gave the best results.

Tests proved that both spontaneous and specific agglutinating power diminish with the age of most strains of the colon-typhoid group. The microscopic is more reliable than the macroscopic method for weak or graphic agglutination work. The macroscopic is most satisfactory for usual work and particularly when many reactions are to be performed. Several tables show tests at different temperatures. Weak agglutination occurs when the bacilli

are heated at 45° C. to 55° C. for two to three hours. Better results were attained at room temperature and 37° C. Since the speed of reaction varies with the strains of bacilli, it was found best to set the tests aside and read them the next day. In serum diagnosis with the Widal test, many different strains should be used, since from one strain alone reliable results cannot be obtained.

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**The Permanence of the Serologic Paratyphoid B Types with Observations on the Nonspecificity of Agglutination with "Rough" Variants.**

*H. Schütz, J. Hyg., 20:330, London, Dec., 1921.*

Observations made upon the constancy of type manifested by a large number of strains during several years of laboratory cultivation. *B. paratyphosus B* with its numerous absorption types was used. A table demonstrates a series of absorptions showing the incompleteness when substrain acts on superserum and completeness when matters are reversed. Even those strains whose serology was registered so long as six years ago still maintain their places in the same absorptive types. Serologically no alteration except in "altitude" within the type has been recorded after laboratory cultivation extending over that period. Two alterations in the serologic nature of certain cultures have been observed. These were due to the development of Arkwright's so-called "rough" variants, and to the degeneration of strains into antigenically less effective "substrains." A series of tables show (1) the affinity of "rough" strains for rough alien serums, which the smooth strains fail to possess, (2) the serologic diagnosis of "rough" strains, and (3) the crossimmunization possessed by various types. Though both of these alterations are variations within the limits of the absorption types, the serologic character of the affected strains may be so obscured that a greater variation than has actually taken place may be ascribed to them, unless certain precautions are observed. There exists a serologic cosmopolitanism among rough cultures. Agglutination tests with such alien species as *B. enteritidis* Gärtnér and *B. paratyphosus A* and *B* are examples of this marked cosmopolitanism.

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**Agglutination Experiments with Polyvalent Colon Serums.**

*Eugen Román, Centrbl. f. Bakteriol., 87:470, Jena, Dec. 30, 1921.*

It is very difficult to pass judgment on the value of a curative serum in those diseases which are named from their clinical symptoms but concerning whose etiology little is known. The author takes up the question of the polyvalence of the serums used for colon dysentery in calves. It is of great importance to determine whether and to what extent the effectiveness of the serum against diseases caused by different strains of colon bacilli is increased by increasing the polyvalence of the serum. The author considers agglutination as an indicator of polyvalence. It is to be assumed that strains which behave differently with reference to agglutination also act differently with regard to serum protective sub-

stances. The author used 6 pathogenic colon strains, part of which he cultivated himself from calves which had dysentery and part of which he obtained from other institutions. Using these strains he prepared serums from rabbits with valences of 1, 3 and 10. Experiments made with them gave the following results: In colon serums the raising of the titer and polyvalence increased the extent of the effectiveness of the serum, but this increase could not be carried to such an extent that the serum could be regarded as specific for all diseases caused by colon bacilli.

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**Action of the Bactericidal Forces of the Blood on Typhoid Bacilli.**

*L. Bogendörfer, Deutsch. Arch. f. klin. Med., 138:120, Berlin, Dec. 20, 1921.*

As typhoid bacilli are not always found in the blood of patients, and if found are only in small numbers, and as they do not grow as well on blood agar plates as on plates to which bile has been added, it would seem that the blood of typhoid patients must contain bactericidal substances. A study of strains from different sources with reference to their resistance to human blood, included (1) strains freshly cultivated from the blood of typhoid patients; (2) from the stools of typhoid patients; (3) from the urine; and (4) different laboratory strains. The blood of the person experimented upon was defibrinated, 6 c.c. of it mixed with 0.1 c.c. of the bacterial emulsion and after six, three and twelve hours, poured on plates. It was found that, *in vitro*, the typhoid bacilli succumbed to the bactericidal forces of the blood. The laboratory stains and those cultivated from the stools died in twelve hours. Those cultivated from fresh blood were more resistant. By the same method it was not possible to demonstrate any increase or decrease in the bactericidal action of the blood in the course of the disease. Exceptions are possibly to be attributed to leukocytosis.

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**The Flocculating Power of Human Blood Plasma.**

*Wilhelm Starlinger, Biochem. Ztschr., 123:215, Berlin, Oct. 25, 1921.*

The writer reports some experiments which he undertook as a result of his studies of agglutination and the phenomena of sedimentation in the case of erythrocytes. The influence of blood plasma, which in that case could be observed very distinctly, would justify an attempt at interpreting the nature of fibrinogen flocculation of plasma. The plasma of pregnant women contains great amounts of fibrinogen, but that of the umbilical cord none at all. But as the sedimentation of red blood-corpuscles depends upon the amount of fibrinogen, and there is a parallelism between sedimentation and flocculation, this alone is sufficient proof of the causal importance of the amount of fibrinogen. The highly re-

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duced surface tension of the plasma of pregnant women also indicates a large amount of components with a high molecular weight.

The experiments were made upon healthy and sick persons. The blood plasma was obtained by powerful centrifugation with sodium citrate in a proportion of 1:4. Precipitation was obtained by the usual methods of fibrinogen precipitation, particularly by adding solutions of sodium chlorid to the plasma in a proportion of 1:1. The indications were read after ten minutes. The experiments show that the flocculation of the blood-plasma depends quantitatively upon the amount of fibrinogen, and it may therefore be used as a measure. Consequently a partial removal of fibrinogen by delicate absorption agents of fibrinogen, like kaolin or bone black, diminishes or completely suppresses sedimentation. Flocculation increases in proportion to fibrinogen content which can also be demonstrated by diluting the plasma with the corresponding serum. In native plasma differences of equilibrium, when plasma rich in fibrinogen shows diminished flocculating power, occur only in exceptional cases. But a distinct obstruction of flocculation can be observed upon addition of acids, alkalis, or neutral salts, on the one hand, or upon raising the temperature or adding Witte's peptone, on the other.

Agar, gum, gelatin and glycocoll cause a pronounced increase of flocculation. These phenomena are explained by Herzfeld and Klinger's theory of solution of colloidal albumin. According to them, the water-soluble lower products of decomposition of albumin serve as intermediate agents for the solution of the entirely insoluble albumin colloids; they attach themselves to other surfaces, and through their power to bind water they create around each individual particle an aqueous tegument which prevents its aggregation with other particles. All influences which destroy or diminish these stabilizing products of decomposition promote the flocculation of albumin. All influences which tend to increase these bodies promote the stability of the solution.

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Blood Concentration.

*W. Nonnenbruch, Arch. f. exper. Path. u. Pharmakol., 91:218, Leipzig, Nov. 4, 1921.*

In order to observe how additions of gum arabic and gelatin to Ringer's solution influenced the exchange between blood and tissue in intravenous injection, the author performed infusion with these substances into the auricular vein in rabbits. The changes in the blood were determined by counting erythrocytes and estimating NaCl content of the serum. Further, residual nitrogen was deducted from total N, and from this albumin was estimated. The total amount of serum may be deduced from the proportion of blood-corpuscles to serum. The initial quantity of blood is assumed to amount to 7% of the body weight. If 40 c.c. Ringer's solution be injected into a rabbit, it is found that a portion has passed into the tissues by the end of the injection. After two hours as many red blood-corpuscles are found in 1 c.c. as before injection,

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but at this time the serum contains more NaCl and less albumin than at the beginning of the experiment. The author obtained the same results with a solution of normosal. The result is not altered materially by the addition of gum or gelatin to 40 c.c. Ringer's solution. These experiments were repeated on nephrectomized animals and no influence on blood values was observed. The day following nephrectomy there is a considerable influx of water, albumin and NaCl into the blood, which is not affected by gum and gelatin. Prolonged plethora is observed only after injection of a high percentage solution of gum. Diuresis is usually arrested by gum gelatin injections, but the injected water may be excreted in two or three hours. After intravenous injection the erythrocytes, relatively as well as absolutely, diminish in number. This occurs more frequently with gum solutions. In other cases the erythrocyte count gave the opposite result. It must be assumed that refraction and the erythrocyte count do not give the same results. Hence, there is no reason for adding a 6% solution of gum arabic to Ringer's solution in order to fill the vascular system. The passage of albumin from the tissues into the blood channel is possibly regulated by the reticulo-endothelial apparatus. Theophyllin would stimulate these cells to increased activity.

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**Blood Concentration. II. The Action of Diuretics of the Purin Series on the Exchange between Blood and Tissues.**

*W. Nonnenbruch, Arch. f. exper. Path. u. Pharmakol., 91:332, Leipsic, Nov. 22, 1921.*

Veil and Spiro found an absolute reduction of the water content of the blood, and an even larger reduction of the sodium chlorid contents in the diuresis due to purin bodies. Their method consisted merely in determining the refractometer values. The author studied the whole question by including continuous erythrocyte counts in his method of examination. A comparison of the results of both methods shows a definite difference between serum albumin values and erythrocyte values. This difference is also found in nephrectomized animals after the administration of theophyllin, theocin and euphyllin, which leads to increase of serum albumin and reduction of erythrocytes. The action on serum sodium chlorid values was slight and irregular. Purin diuresis cannot be explained by means of such quantitative estimations of blood values or of their alterations. The determining factors in purin diuresis, apart from the condition of the kidney, are the condition of the tissues, the amount of water and salts in tissues, and the combination of water in blood and tissues.

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**Analysis of a Volume-Curve of Blood Corpuscles in Hypertonic Solutions, Making the Differentiation of Osmotic and Chemicocolloidal Changes in Volume Possible.**

*Takeo Takei, Biochem. Ztschr., 123:104, Berlin, Oct. 25, 1921.*

Pharmacologic and immunologic influences do not always combine with the effects of the suspension media used, and the effect of many of these products depends entirely upon the composition of the medium. For instance, washing the blood-corpuscles with solutions of pure sodium chlorid considerably lowers the osmotic resistance of these corpuscles. The complement in salt-free isotonic solutions is not capable of activating hemolytic amoebocytes. This phenomenon of complement activation led to the division of the complement into a middle part (globulin fraction) and an end part (albumin fraction). Blood-corpuscles react differently in salt and sugar solutions when hemolyzed by cobra venom. This occurs only in salt solutions to which lecithin has been added. In sugar solutions hemolysis takes place without an addition of lecithin. It is known that in isoosmotic solutions the volume does not need to be the same, and this is explained by the osmotic and chemicocolloidal theories. The first theory requires the existence of a comparatively semipermeable corpuscle-membrane. The latter explains the phenomenon of change in volume and hemolysis as the direct result of turgescence and absorption. Late investigations indicate the existence of an especially differentiated tegument, produced through surface condensation. For those phenomena of change in volume which last only a short time, the initial difference in osmotic pressure might be of importance. Whenever the corpuscles are allowed to remain in the experimental medium for a considerable time, the chemicocolloidal influences will always enter into action. If it is desired to determine the osmotic and chemicocolloidal influences at the same time, this can be done only if it is possible to increase the action of both factors. This is the case when examining the volume of blood corpuscles in strongly hypertonic solutions. The present method of investigation is valuable, as electro-endosmosis is of primary importance and changes in permeability occupy a secondary place.

The volume of the corpuscles was examined in glucose and different salt solutions by the following method: Fresh rabbit blood, 0.08 c.c., was well mixed in Hamburger's conchematoctrites which had been previously mixed with 1 c.c. of glucose solution, and centrifugation effected until it reached a constant volume. The glucose solutions, before being used, were converted into normal volumes of their own plasma at 100° C. Human, rabbit and bovine blood, suspended in hypertonic media, shrink according to the external osmotic pressure, provided this external pressure is not more than 4 times greater than normal isotonia ( $\Delta-2^{\circ}$ ). The decrease in volume depends exclusively upon direct osmotic withdrawal of water. Whenever osmotic external pressure becomes 4 times greater than normal isotonia, a sudden increase in volume of the corpuscles occurs, until it almost reaches the isotonic volume. This increase is due to a swelling of the colloids of the corpuscles,

which is probably caused by the ions of the internal salts of the corpuscles. Osmotic shrinking is reversible. The swelling is irreversible, because a sudden access of water always causes hemolysis. The writer also investigated the permeability of the corpuscles for ions in concentrated sugar solutions, by determining their electric conductivity. The viscosity of the corpuscular colloids was measured with a viscostalagmometer at a constant temperature. The volumes of the corpuscles in hypertonic media can be compiled in a curve which has a constant form and does not depend upon the chemical composition of the medium, but only upon the osmotic pressure. Solutions of alkaline chlorids and alkaline sulphates, of glucose and glucose in Ringer's solutions, which are all isoosmotic, have an identical curve. No swelling occurs in hypertonic glucose serum, because in this medium most of the water is tied up in chemicocolloidal combinations. The results are compiled in curves and it may be possible to use these volume curves in clinical examinations. The turgescence curves may be of especial importance, as aged blood-corpuscles are distinguished by their greater, and the younger corpuscles by their lesser, inclination to swell.

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**Quantitative Effect of Some Coagulation Factors upon the Coagulation of Blood.**

*Ludwig Heller, Biochem. Ztschr., 123:90, Berlin, Oct. 25, 1921.*

It is a known fact that diluted blood does not coagulate. It was found that coagulation of the blood depended upon the concentration of the active substances. The writer investigated the substances which prevent a coagulation of diluted blood, particularly the effect of calcium chlorid and of sodium chlorid, as these two bodies are the characteristic factors of coagulation from the chemical point of view. They exercise considerable influence upon the coagulation of blood, and their effect again depends considerably upon their concentration. The effect of dilution upon coagulation was investigated with human blood, as no quantitative data concerning it are available.

First of all the writer determined the minimum quantities required to produce coagulation with varying concentrations of the blood, using physiologic solutions of sodium chlorid. In addition, he determined the minimum quantities required when varying the concentration of calcium chlorid, using 0.5% solutions of sodium chlorid and blood in dilutions of 1:150, 1:200, 1:400 and 1:600. He endeavored to determine the most favorable concentration of sodium chlorid using calcium chlorid in a dilution of 0.01% and blood 1:200. Lastly he tried to determine the lowest possible blood concentration, when using calcium chlorid in a dilution of 0.05% and sodium chlorid of 0.5%.

The blood investigated was taken from the median vein. The experiments show that the lowest possible concentration of the blood is 10%. The lowest possible concentration of calcium chlorid, using blood in a dilution of 1:200, is about 0.005%-0.006%. The higher the concentration of the blood, the lower is the con-

centration of calcium chlorid required to cause coagulation. Using a blood concentration of 0.5% and a calcium chlorid concentration of 0.01%, the concentration of sodium chlorid has to be 0.6%, the lowest limit of blood concentration at which coagulation still occurs is about 1:800. These values are not absolute and vary considerably with the methods used. But using the same experimental arrangement for different cases, it is possible to obtain values which can be very well used for purposes of comparison. In two cases of jaundice the concentration of calcium chlorid required was much higher than in the case of normal blood. In two cases of a light attack of jaundice, the blood concentration required was higher than in the case of normal blood. In cases of syphilis with secondary phenomena and positive Wassermann reaction, the blood concentration required was on an average 1.62 times lower than in the case of normal blood. Comparing this figure with the amount of fibrinogen contained in syphilitic blood as determined refractometrically by Winternitz, and the value obtained for it (154), it is found that these two different methods give about the same values. This proves that the present method is suited to indicate the increased fibrinogen contents of syphilitic blood. In order to avoid an influencing of the coagulation process by changes in temperature, admixture of tissue fluids, duration of blood removal, shape, material and size of the vessel, etc., the writer proposes to construct a dilution syringe which would make it possible to obtain the blood diluted to the desired degree directly upon removal from the source of supply. The reaction should be allowed to take place in a thermostat. These methods would then be more exact than the time determination method; and they would also have the advantage of indicating the changes occurring the individual coagulation factors, particularly the fibrinogen and the thrombin factor.

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**Changes in the Refractive Index of the Blood Serum of the Albino Rat with Temperature.**

*F. S. Hammett and Ida Teller, J. Biol. Chem., 50:47, Jan., 1922.*

The serums for examination were taken, under ether, from the ventricles of mature albino rats. Blood was collected from the beating heart in small test-tubes which were tightly corked at once and allowed to stand until coagulation was complete. The serum was separated by centrifuging for one-half hour at the end of which time the supernatant serum was poured into another small test-tube and again centrifuged for half an hour. During the centrifuging process the tubes were tightly corked, to prevent loss of water by evaporation. The instrument used by the authors was a Pulfrich refractometer, which was connected with the temperature regulating apparatus described by Reiss. Readings were made to tenths of a minute. It has been previously observed that the value of the refractive index of the serum of the albino rat varies with the age and to a less degree with the size of the animal. The animals in this series of experiments varied in size, although they were all about the same age. These differences in size re-

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sulted in differences in the initial refractive index of the serum, but in order that the values might be brought to a common basis for purposes of study, the percentage difference between the refractive index of the serum and that of water at the initial temperature of observation was determined. The subsequent observed indexes for the serum at the different temperatures were multiplied by this factor, thus making the curve of the change in refractive index with temperature of the serum comparable with the temperature curve of water, the solvent. Any changes in the refractive index due to the influence of temperature on the serum constituents other than water would then be shown by a deviation of the curve for the serum from that for water. The tabulated results show that the serums fall into 2 groups with respect to their accommodation to the water curve. In group one the changes in the refractive index with temperature are solely due to the changes in the refractive index of the solvent, water. This was found to hold, up to a temperature of about 29°. Above this point there was indication of a tendency for the refractive index of the serum to increase more than that of water. In group two the curve of the change of refraction with rising temperature falls away from that of water, which demonstrates a participation in the response of serum constituents other than the solvent, water. The authors state that it is certain that in this series the factors of body length, body weight, age, and water content of the serum both before and after the experiment, and the previous state of digestion and absorption, are not the causes of the difference between the 2 groups.

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**Influence of Metals upon Serums.**

*Leo Hess and Rudolf Reitler, Biochem. Ztschr., 123:51, Berlin, Oct. 25, 1921.*

When suspensions of red blood-corpuscles of sufficient concentration are introduced into isotonic solutions of sodium chlorid, which has previously been in contact with metals, hemolysis occurs. If the erythrocytes are suspended in serum instead of sodium chlorid, this interferes with hemolysis, even if, in place of sodium chlorid-metal, serum-metal was used. In the latter case it was possible to observe precipitation of the serum by the metal. These experiments seem to be of importance in connection with the interpretation of the complement of the serum.

When clean metallic strips were introduced into undilute native serum, after a few days at 0° C., a whitish precipitate was formed which is insoluble in solvents of lipoid. Human serum is mixed with physiologic solutions of sodium chlorid of 10, 15, 20%, etc., copper is added, it is kept in an icebox for twenty-four hours and then examined.

It was found that under otherwise identical conditions fresh serum was precipitated at higher concentrations than older serum. This indicates that the faculty of being precipitated recedes with age. It might be possible to use for diagnostic purposes the absolute limit of precipitation in connection with the albumin content of the serum at a given moment. At all events, the undoubtedly increased precipitability of

the serum of persons affected with cancer is remarkable, and invites further investigation. The writer also investigated the relative precipitability of native serum containing its complement and of inactivated serum deprived of its complement by heating for half an hour at 56° C. It was found that an active serum could be more easily precipitated than an inactivated one. Thus the difference between native and warmed or aged serum, the so-called complement, the existence of which was indicated in biologic experiments, finds its physical and chemical counterpart in a different behavior toward the precipitating action of metals. Serums with complement can be more easily precipitated than those deprived of it. In experiments with a hemolytic system the complement of which was subjected to the influence of copper, no lysis occurred. The solubility of erythrocytes is not influenced by contact with copper solution. But a high degree of dilution, reaching nearly the titer limit, causes a little weakening of the amboceptor, which manifests itself by an incomplete lysis, but it seems impossible to eliminate its effect completely, as can be done in the case of the complement.

The failures of internal antisepsis are due to the high organotherapy of the antiseptic, which does not enable the required quantities of it to be used and thus makes it impossible to attain a concentration required for the disinfecting effect. Success is also prevented by the fact that the bactericidal power of the disinfectant is extremely weakened in the colloidal medium of the serum. For purposes of internal disinfection there is only one possible way to bring the active metal into contact with the bacteria, and that is by fixing them upon intermediate bodies which cannot be deviated by the serum; then according to Ehrlich's interpretation the intermediate bodies would be split, which would bring the metal in oligodynamic dilution into contact with the bacteria. The experiments show that mixing copper solution with serum containing amboceptor diminishes the bactericidal effect of copper only very slightly, but guinea-pig serum, not deprived of its complement and diluted to the same extent diminishes the effect of copper considerably. As, on the other hand, a combination of copper, complement and amboceptor does not bring into action any immunity bodies, but the entire effect is produced by copper alone, it seems probable that it is not only the surplus of free copper which produces all the observed effects, but that the copper combined with complement, at least partly, is brought to bear upon the germs by means of the amboceptor.

It was found that the oligodynamic action of copper was greater in serum when the metal had been previously combined with some specific system of immunity bodies than in serum where the metal was used in a free state.

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**Solubility of Carbon Monoxid in Serum and Plasma.**

*H. R. O'Brien and W. L. Parker, J. Biol. Chem., 50:289, Jan., 1922.*

Method for the determination of carbon monoxid in serum and plasma. Beef, sheep, and human serums, and beef plasma were saturated with the gas at 15°, 20°, 25°, 30°, and 37° C. Compatible figures

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were obtained. These were of the same magnitude as those of the known solubility of carbon monoxide in water, but only about three-fourths as large as the latter. The method was checked by a determination of the solubility of carbon monoxide in distilled water. The solubility figures in serum and plasma were found to be identical. The authors did further work on the solubility of carbon monoxide by exposing the serums and plasma to mixtures of 1 to 10% carbon monoxide in air. The amount of this gas dissolved under those conditions is so very small that in calculating results in cases of poisoning under ordinary conditions, no allowance need be made for carbon monoxide dissolved in the serum.

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**The Quantitative Estimation of Bilirubin in Blood Serum.**

*Pál Ormos, Orvosi hetil., 65:429, Budapest, Dec. 4, 1921.*

In jaundice the cutaneous tissue is permeated by the bilirubin circulating in the blood serum. The degree of jaundice is judged by the discoloration of the skin and by the appearance of biliary pigments in the urine. Neither symptom supplies an adequate standard for measuring the amount of bilirubin in blood serum, inasmuch as albuminoids in the latter absorb much bilirubin and its passage into the urine takes place only after a certain concentration has been reached. From this it follows that the methods hitherto employed must fail to disclose the presence of already existant hyperbilirubinemia. The quantitative estimation makes it possible to detect even a small increase in bilirubin and, further, to determine the exact degree of jaundice or bilirubinemia. The reaction is based on the formation of a new compound of bilirubin with diazo-salts, which is red in neutral, blue in acid and bluish green in alkaline solution. Its spectrum shows characteristic absorption bands. The reaction is applied in alcoholic solution. Albuminoids are precipitated by adding 2 parts of alcohol to 1 part of serum. This mixture is centrifuged and 1 part of the liquid so obtained receives the addition of  $\frac{1}{4}$  part freshly prepared diazoreagent. In the presence of much bilirubin we obtain a red reaction; with little bilirubin it is pink. Slight turbidity is due to insoluble fatty acids which are entirely redissolved by heating, or by adding a few drops of ether, or  $\frac{1}{2}$  part of alcohol. The quantitative estimation is effected by comparing the color reaction obtained with definite quantities of materials, with the color produced by a bilirubin solution of known strength. The diazo reaction enables one to determine whether bilirubin is present in serum under normal conditions in which the maximum concentration corresponds to dilutions of 1 in 200,000. Higher concentrations are found only in pathologic conditions, excepting those rare cases in certain families in which physiologically increased bilirubinemia is in evidence. The amount of bilirubin in serum may be increased (1) by increased formation in the reticulo-endothelial apparatus, increased supply of hemoglobin, disintegration of erythrocytes due to pernicious anemia, hemolytic jaundice and paroxysmal hemoglobinuria; (2) as a result of diminished secretory power of liver cells, or resorption by liver cells (atrophia hepatitis acuta, primary or secondary, due to congestion at the beginning of decompensation of defects), in this case the functions of the liver cells are impaired;

(3) by a combination of (1) and (2); (4) by mechanical stoppage of the biliary ducts (cholelithiasis, catarrhal jaundice). The author deems the quantitative estimation of bilirubin of importance in: (1) Cardiac decompensations. In so far as these are limited to the right side of the heart, bilirubin is an early indication, as it appears in the serum much sooner than in the urine. (2) Pernicious anemia. (3) Cholelithiasis, cholecystitis, if the patient exhibits no objective symptoms apart from pain.

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**Reaction Type of Biliary Pigment and the Quantitative Proportions of Bilirubin and the Cholesterin in the Blood in Different Forms of Jaundice.**

*F. Rosenthal and K. Meier, Arch. f. exper. Path. u. Pharmakol., 91:246, Leipzig, Nov. 4, 1921.*

In a previous communication the author had stated that those forms of jaundice which are accompanied by biliary obstruction show hypercholesterinemia, in contradistinction to forms depending on blood disintegration. Here, jaundice of the new-born, that due to toluylendiamin and phenylhydrazin poisoning, and that due to phosphorus, is dealt with and may be thus summarized: Jaundice of the new-born is characterized by the absence of hypercholesterinemia, as well as by a strongly retarded direct diazo reaction. Toluylendiamin jaundice in the dog is characterized by the positive direct diazo reaction and considerable hypercholesterinemia. It manifests itself from the beginning as jaundice with cholemic blood constitution and, therefore, shows wholly different blood chemism to the purely dynamic bilirubinemic forms of jaundice in human beings. In toluylendiamin jaundice in the cat the serum also shows a prompt direct diazo reaction, but no cholesterol increase. The intensity of blood jaundice is not related in any way to the degree of blood disintegration. Phenylhydrazin produces very slight blood jaundice in the dog even with excessive anemia. The biliary pigment in the blood has the moderately retarded direct reaction type. Blood jaundice with phenylhydrazinemia runs its course without cholesterol increase in the blood, resembling in that respect the closely related jaundice of human pernicious anemia. Phenylhydrazin poisoning in the rabbit is not attended by bilirubinemia. The considerable lipoidemia observed in the phenylhydrazinemic rabbit would seem to indicate probable important differences in lipoid metabolism between carnivora and herbivora, and that the rabbit's liver is physiologically attained to limited functional capacity in respect to cholesterol elimination. Phosphorus jaundice in the dog belongs to the jaundice group showing cholemic blood constitution, even with a prompt direct diazo reaction in the serum and with symptoms of moderate hypercholesterinemia. The absolute threshold for the urine capacity for bilirubin in the dog lies extraordinarily low, which is evident in hunger bilirubinuria, in toluylendiamin jaundice and phosphorus jaundice. Even when mere traces of biliary pigment are found in the serum, bilirubin may be detectable in larger amounts in the urine. A prompt direct diazo reaction in the serum is not related to hypercholesterinemia of the icteric serum, which is proved by toluylendiamin jaundice in the cat, as also by phosphorus jaundice in the dog.

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**On the Distribution of Chlorin in the Blood.**

*S. van Creveld, Biochem. Ztschr., 123:304, Berlin, Nov. 5, 1921.*

The distribution of chlorin between plasma and corpuscles was investigated in arterial and venous blood. The experiments demonstrated that blood-corpuscles in flowing blood always contain chlorin, and they showed the different distribution of chlorin in plasma and corpuscles in arterial and venous blood. From the values obtained for the whole blood it is evident that a further exchange between blood and tissues must take place. If the plazma and corpuscles be separated directly after the blood is obtained, coagulation being prevented, the corpuscles at times contain no chlorin whatever. If both plasma and corpuscles be separated, after total or partial coagulation has set in, a fairly constant proportion is found. In vivo the proportion is not constant and it is certainly higher in venous blood. It seems preferable, therefore, to estimate chlorin in the whole blood instead of, as heretofore, in the serum, owing to the fluctuating values under different conditions. The proportion between the small amount of indiffusible chlorin and the diffusible chlorin is said to depend on the concentration of hydrogen-ions in the serum. In serum, nearly the whole of the chlorin is probably in the free state, while in plasma a considerable portion is chemically combined. Such a chlorin compound was considered by Falta to occur as a chlorin-fibrinogen combination in the plasma. Comparative determinations of chlorin in plasma and in the aqueous humor, which latter behaves as an ultrafiltrate (dialyzate) of the blood, have demonstrated the nonexistence of such a chlorin-fibrinogen compound.

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**The Production of Hunefeld-Hensen Figures in Frog Blood  
(by the Addition of Small Amounts of Water).**

*Joh. Brodersen, Anat. Anz., 54:385, Jena, Nov. 3, 1921.*

To study the Hunefeld-Hensen phenomenon, Brodersen constructed small mica chambers, which enabled him to renew the examining fluid or replace it by another, without disturbing the examination. He experimented with *Rana temporaria* and with salamanders.

Upon the addition of distilled water, the nuclei of the red blood-cells first become more distinct and more refractive in their contour and in the various granules of their protoplasm. When the action of distilled water, or of hypo-isotonic salt solution, is continued, the nuclei become less refractive, the cell approaches more and more a spherical form, and the nucleus finally disappears. Under the following influences the cells may assume an ellipsoid form: (1) 0.01% aqueous solution of NaOH—the shape slowly returns to spherical; the same is true of (2) N/2000 aqueous solution of HCl—a lasting change from the ring form to the ellipsoid, that is, true Hunefeld-Hensen figures, takes place only when the red blood-cells which have been swelled in water, are treated with (3) NaCl in 0.3-0.9% solutions—the place of NaCl may also be taken by a corresponding solution of other neutral salts or by an isotonic cane-sugar solution.

Measurements of the cells have demonstrated that under the influence of water the cell increases in size and will return to its original

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volume under the action of the salt solution. The nucleus swells during the first stage and retains this size in the second. If water is again allowed to act upon the Hunefeld-Hensen figures, they change to a spherical form. This process may be repeated several times with the same cell, but eventually the hemoglobin diffuses out. Leukocytes may also be made to assume the ring shape. The Hunefeld-Hensen figures also result if swelling of the nucleus is prevented by acidulating the first fluid used in the experiment. A small amount of cellsubstance remains in the peripheral, clear mass of the Hunefeld-Hensen figures, between the layers of cell membrane.

Brodersen does not accept the opinion of Meves, that distilled water produces a precipitate membrane on the surface of red blood-corpuscles, as in that case no retrograde changes could ever take place in the Hunefeld-Hensen figures. Probably no satisfactory explanation of the appearance of the Hunefeld-Hensen figures can be given, but it is reasonable to assume osmotic processes, such as take place in vegetable cells during plasmolysis. In the latter case the membrane itself is the site of semipermeability.

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**The Measurement of Red Blood-Corpuscles by Means of the Phenomena of Diffraction.**

*F. L. Bergansius, Pflüger's Arch. f. d. ges. Physiol., 192:118, Berlin, Oct. 29, 1921.*

Pijper has described a diffraction micrometer for throwing a parallel bundle of light, produced by a condenser lens from a strong arc-light, through a single layer of blood-corpuscles. Such a layer is produced by placing a strongly diluted emulsion of blood between 2 pieces of plate-glass separated on one side by a cover glass so that they inclose a wedge-shaped space. If a proper degree of dilution is applied, the bottom of this wedge-shaped space will be entirely covered in one place by blood-corpuscles adjoining each other without overlapping. An achromatic lens is fixed below the wedge together with a white screen (at a distance equal to that of its focus), on which appears a luminous image of the source of light, surrounded by 2 or more colored rings (violet within and red without), the diameter of which increases in inverse proportion to that of the blood-corpuscles. The author modified this apparatus by employing a small source of light and a weaker condensor, producing a reduced image of the former—a spectacle lens of +1.D serving as condensor and one of +5.D for the formation of the image. The phenomena in question, which belong to the group of Fraunhofer's phenomena of diffraction, are made the subject of a theoretical discussion, and the conditions governing the size of the rings are deduced. The blood-corpuscles must not be looked upon as opaque screens; indeed, the phenomena of diffraction are produced principally by the light passing through them.

Although the exactness of the measurement amounts at most to 1-2%, it may be considered as sufficient for clinical and physiologic purposes—the more so as the diameters of many thousands of erythrocytes may be ascertained in this way by one measurement.

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**Schüffner's Granules in the Red Cells of Tertian Malaria.**

*C. Gil, Arch. cardiol. y hematol., 3:12, Madrid, Jan., 1922.*

The origin of the granules is not entirely clear. The author had occasion to examine blood derived from infection with *Plasmodium vivax*. If the smear is washed in water the granules are caused to disappear but the hemoglobin is lost more rapidly. The granules usually appear after several of the tertian crises but may be present, in extensive infections, from the first. The granules do not indicate young red cell formation. They occur with *Plasmodium vivax*, which produces relatively slight blood changes, but not at all with *Plasmodium malariae*, which causes profound disturbances of the blood and other structures. With Neumann and Mayer, the author thinks that the granules are produced by the action of the parasites. They increase in size according to the development of the parasite within the red cell. There is a certain relation between the number of granules and volume of the parasite. As the parasite enlarges, the granules become more distinctly basophilic. The hemoglobin of the red cell diminishes as the number, size and basophilic reaction of the granules increase. The granules appear to consist of hemoglobin or a hemoglobin derivative. A very pretty plate accompanies the article.

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**Experiments upon the Adsorption Power of Hemoglobin to Erythrocytes in Individuals of Different Ages.**

*Frantisek Luska, Časop. lék. česk., 60:881, Prague, Dec. 31, 1921.*

The subject of an increased predisposition of the delicate child organism toward infectious diseases is often discussed; it is attributed to inactivity of the tissues and to the lack of the power of forming specific antibodies. However, this is not absolutely true, as an active antibody formation frequently does occur and the total injury to the infant is nevertheless severe. The adsorption relationships of hemoglobin were studied to elucidate this phenomenon. Some authors claim that the hemoglobin does not adhere as closely to the erythrocytes of infants as to those of adults, but experiments show that the upper limit of hemolysis occurs at 0.45% sodium chlorid in the new-born, just as it does in adults. The resistance of the lipoid erythrocyte membrane does not come into consideration in the hemoglobinemia of the new-born. The hemoglobin cannot be chemically bound in the erythrocytes; nor can it be contained in a free state in the stroma spaces; therefore it must be in some relationship with the plasma substance or membrane, respectively, which is subject to quantitative changes. This is the adsorption, the tendency of a substance of lower surface tension, which finds itself in a colloidal solution, to attach itself to a great extent to the surface of parts of the colloidal solution.

The results of the series of experiments *in vitro* were: (1) The adsorption of hemoglobin through animal charcoal increases in the presence of a toxin (bouillon filtrate with staphylotoxin). (2) An acid reaction of the solution increases the adsorption power of the hemoglobin through animal charcoal. This is important, as the alkalescence of the blood-serum slowly increases in extra-uterine life, in contradistinction to the concentration. (3) The slightest adsorption

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appears in such a concentration as occurs in very young individuals; in those cases in which the concentration corresponded with the findings in the adult, the adsorption was greater. (4) The effect of a hemolytic toxin upon erythrocytes: (a) the optimal staphylotoxic hemolysis occurs in a medium of minimal alkaline reaction with a concentration in accordance with the individual with the youngest serum; (b) the intensity of the staphylotoxic hemolysis sinks with the increasing alkalinity of the medium; (c) the resistance of the erythrocytes of young individuals toward staphylotoxin is lower than that of older individuals.

From these findings the conclusion can be drawn that the more marked staphylotoxinhemolysis with a minimal alkalinity of the medium is the result of the lesser power of adsorption of the hemoglobin toward the stroma or the membrane of the erythrocytes, respectively, and that all remedies which produce the elimination of hemoglobin from the erythrocytes, independently of osmotic influences, will have a greater effect in a minimal alkalinity (that is, in young individuals).

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**The Effect of Some Electrolytes and Anelectrolytes upon the Rapidity of Sedimentation of the Red Blood-Corpuses of the Horse.**

*J. Runnstroem, Biochem. Ztschr., 123:1, Berlin, Oct. 25, 1921.*

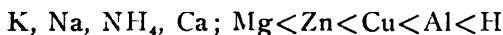
Fahreus was the first to observe that the stability of red blood-corpuses was diminished during pregnancy and different pathologic conditions. He determines the stability of the red blood-corpuses by measuring at certain times the plasm or serum which is free from red blood-corpuses, due to their sedimentation. The object of the present investigation is to study the influences which different electrolytes and narcotics have upon sedimentation, and also to derive some additional knowledge concerning the surface layer of cells.

The writer used defibrinated horse blood exclusively. The serum was centrifuged and the red blood-corpuses were washed twice with a 0.9% solution of sodium chlorid, or with Ringer's solution, sometimes with isotonic sugar solution. First he investigated the influence which the different ions exercised upon sedimentation of the red blood-corpuses, then the influence of salts upon agglutination of red blood-corpuses in acid solutions, then the rapidity of sedimentation and the resistance of the red blood-corpuses. It was found that a remarkable analogy existed between the rapidity of sedimentation and hemolysis of the red blood-corpuses by marked decrease of tension.

The effects of electrolytes upon the stability of red blood-corpuses could probably be best explained by the electric theory of agglutination, according to which the red blood-corpuses carry a weak charge in electrically poor solutions; this load charge increases with increasing content in alkaline salts. The higher resistance to agglutination by hydrogen ions, with increasing sodium chlorid content, is due to an increased negative charge of the red blood-corpuses due to absorption of anions. Probably the red blood-corpuses absorb

the anions, but not the kations of the investigated electrolytes, but some investigators think that the electrolytes, particularly the anions, are absorbed by the surface layer of the red blood-corpuscles.

If the absorption of anions has a stabilizing effect upon the red blood-corpuscles, the addition of acids should produce a similar effect. The effects of the addition of hydrochloric acid or other acids to a solution of gelatin show that the red blood-corpuscles act differently in the presence of different anions; sulphuric, hydrochloric and hydrobromic acid have a stabilizing effect, while hydroiodic and prussic acid increase the rapidity of sedimentation. The agglutinating effect of salts of the heavy metals may be due to an absorption of positive ions by the surface of the red blood-corpuscles. As far as could be ascertained, the absorption of kations takes place according to the sequence of Rona and Michaelis:



The sequence of ion absorption depends upon concentration; the addition of hydrochloric acid may change the sequence of anions. An increase in the amount of alkali salts contained in the suspension medium of the red blood-corpuscles increases the number of hydrogen ions necessary for an agglutination of the red blood-corpuscles. The lower the salt concentration, the more pronounced is the colloidal effect; thus an increased concentration of colloids acts like a lowering of salt concentration, and it produces the same effects: the formation of coin-rolls and of flocculi (or clumps) becomes very pronounced, that is, the flocculating power of the colloids is increased.

The writer defends the electric theory of flocculation. The effect of ions is considered to be the result of their absorption by the surface of the red blood-corpuscles. The effect of colloids (serum, gelatin, etc.) is considered as a combat with the electrolytes for the possession of the surface of the red blood-corpuscles.

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**A Note upon the Significance of Digestion Leukocytosis.**

*D. Noël Paton, Lancet, 202:15, London, Jan. 7, 1922.*

According to Paton's observations, the blood of the dog during digestion contains about 30,000 leukocytes per cubic millimeter, i. e., 30,000,000 per cubic centimeter. The increase is sometimes as high as 140%. Taking the diameter of the leukocyte at 10 microns and assuming it to be spherical, its volume may be calculated as  $0.00000052$  c.c., i. e.,  $520 \times 10^{-9}$ . Hence the volume of leukocytes passing through the intestine in the six hours of digestion is  $54,000 \times 30 \times 10 \times 520 \times 10^{-9}$  or 842.4 c.c., which (taking their specific gravity as that of water) gives 842.4 gm., an amount amply adequate to deal with the largest possible absorption of protein. The ratio between the volume of leukocytes and that of the blood is 842.4:54,000, or 1.6%, a value such as might be expected during a leukocytosis of about 100%.

**1f. PATHOLOGY**

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**Some Cases of Acardia.**

*Gruber, Beitr. z. path. Anat., etc., 69:517, Jena, Oct. 13, 1921.*

(1) Holo-acardius amorphus acephalus, abrachius pseudomonopus: malformed fetus 20 cm. long, expelled after the birth of a well-developed twin. Spinal column, ribs and pelvis present.

(2) Holo-acardius amorphus paracephalus, dipus, monobrachius: malformed fetus 27.5 cm. long, with fairly well marked lower extremities and a penis-like structure in the genital region. Spinal column and pelvis present. In the skull, defect of the squama occipitalis, the left squama temporalis and almost complete absence of facial bones.

(3) Hemi-acardius monobrachius: malformation, 32 cm. long, head attached to trunk; two legs; and a stump in place of the right arm. Spinal column and ribs present, pleural sacs, lungs and muscular diaphragm missing; rudiments of liver and pancreas, a bilocular anlage of the heart can be demonstrated. Numerous intestinal atresias, horseshoe adrenal, atresia of the ureter, the anus and the choana, defects of the eyes, cerebrum and right ureter. In this case differentiation has progressed quite far, although the malformation of the cervical region must have begun in the second or third week of embryonic life. In the other cases, which showed no definite organs, or only rudiments, disturbances of development must have begun much earlier.

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**Case of Holoacardius Eumorphus.**

*W. Strakosch and H. E. Anders, Arch. f. Gynäk., 115:408, Berlin, Nov. 29, 1921.*

Acardia occurs only in twins, one of them having no heart at all, or only an imperfectly developed one (holoacardius, hemiacardius). According to the theory of Ahlfeld, Claudius and Schatz, this is a result of the formation of anastomoses in vessels of the placenta, and of transfusion from capillary villi, which causes a partial or complete reversal of the blood circulation in one of the twins. This leads to a defective formation of heart tissue, or, in case such tissue exists already, to its atrophy or degeneration. It also disturbs the development of certain organs, or even of the whole fetus, usually combined with pronounced dropsy, caused by an obstruction of the venous circulation. This theory is opposed by the one of Breus, which is supported by Bauereisen, Panum, Daresto and Meckel. Breus considers acardia to be caused by a disturbance of embryonic development, the primary cause of defects or absence of development of the heart. The existence and development of the fetus is only rendered possible by the formation of anastomoses in the placenta. This malformation of a twin without a heart may attain such extreme proportions that the result is merely a formless lump suspended by the umbilical cord, sometimes provided with fragments of extremities (acardiatus amorphus), between which and teratoma there are transition forms.

On account of their rare occurrence these acardiac monsters are of very little importance in gynecology. The writers discuss one case

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from the clinical and pathologic-anatomic point of view. This case is remarkable for the fact that the malformation had a normal appearance, although it was distorted by considerable edema. Like all similar cases, it occurred in twins. The second twin was normal, but lived for three days only, and apparently died of lack of vitality. The internal organs were lacking in the malformation, or showed very defective development. Heart, liver, spleen, stomach did not exist; there was atresia of the anus, rectum and vagina. These facts lead to the conclusion that this malformation must have started at an early stage of embryonic development. The etiology of these cases is not clear. The case under discussion is remarkable for its almost normal exterior appearance, and, therefore, to the already existing groups of holoacardii acephali, acorni, amorphi, it is necessary to add the group of holoacardii eumorphi.

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**Partial Persistence of the Left Superior Vena Cava Together with an Anomaly of the Pulmonary Veins.**

*Elisabeth Cords, Anat. Anz., 54:491, Jena, Nov. 30, 1921.*

In the case of a man 34 years old, who succumbed to influenza, Cords has found a vein rising from the medioventral surface of the upper lobe of the left lung and running toward the cranium, terminating in the left angulus venosus. Dorsally the accessory azygos vein emptied into this vena cava. The other veins presented a normal development, except that the left superior pulmonary vein was absent. At the point at which it normally enters the auricle there appeared a slight dilatation of the auricular wall, possibly the point of entry of a rudimentary left superior pulmonary vein. With the exception of a small patent oval foramen, the heart was normal. A ligament of the left vena cava could not be demonstrated. The blood, which was oxygenated in the left auricle, did not, therefore, enter the peripheral circulation, but passed through the abnormal vena cava, through the left innominate vein into the right auricle.

This case exhibits a number of instances of arrested development in the region of the venous circulation. A portion of the left anterior cardinal vein persisted, as well as the upper segment of Cuvier's duct, in the form of an incomplete left superior vena cava. In addition, there was persistence--although incomplete--of the upper segment of the left posterior cardinal vein. The very rare malformation of the entrance of a pulmonary vein into the system of the vena cava can be explained by assuming that for some reason or other the circulation of the blood in the upper lobe of the left lung was interfered with during embryonic life, causing the central portion of the left superior pulmonary vein to atrophy. The anastomoses normally existing between pulmonary and bronchial veins, and the communication of the latter with the primitive venae cavae, were sufficiently developed to answer the increased demands after birth.

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**Sagittal Section of a Primipara Dying During the Stage of Dilatation.**

*v. Jaschke, Beitr. z. path. Anat., etc., 69:532, Jena, Oct. 13, 1921.*

The most interesting finding in the section was the development of a large fetal head tumor, although the os was nearly closed. This is explained by the fact that, in consequence of the narrowed pelvis, the skull at the inlet was exposed to the direct action of the bony brim of the pelvis through the thin uterine wall. When the skull does not occlude the pelvic inlet during the stage of dilatation, no head tumor will develop before complete dilatation of the os.

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**A Sacral Teratoma Containing an Embryonic Scapula.**

*Albert H. Montgomery, J. A. M. A., 78:416, Feb. 11, 1922.*

The origin of sacral teratomas is not always definite. Roentgen ray examination is of considerable assistance in diagnosis. The sacral location is always suggestive of teratoma, but often the diagnosis will remain uncertain without a careful exploratory operation. The writer reports a case of a white boy, aged 5 months, who was apparently normal except for a pedunculated tumor about the size and shape of a pear attached like a tail in the median line at the lumbosacral portion of the back. Roentgenograms showed an irregularly shaped, dense, bone-like shadow, not attached to the spine, lying longitudinally in the center of the lighter shadow of the tumor. No defect was demonstrable in the bony outline of the vertebrae. The tumor was removed and found to consist of coarsely lobulated fatty tissue. On incision longitudinally into the mass a hard substance was found intimately adherent to this tissue, and a well formed right scapula was disclosed. The teratoma in this case was possibly of monogerminal origin, as it occurred in a location somewhat near the scapula and was attached by a fatty pedicle to a probably closed fissure in the spine. However, it was not close enough to the scapular origin definitely to rule out the possibility of a bigerminal growth. The child had 2 normal scapulas demonstrable in the roentgenograms and by palpation.

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**Atavistic Anomalies of the Extremities of the Limbs.**

*H. Brodier, Paris chir., 13:409, Oct.-Nov., 1921.*

Case I.—In both hands a supernumerary finger adherent to the proximal third of the fifth finger, which was made up of 2 small phalanges united without an articulation. Case II.—Supplementary thumb on the external border of the first phalanx of the thumb of the left hand. Radiography showed the existence of an elongated distal and a short proximal phalanx. There were 2 articulations, one between the 2 phalanges and the other between the proximal phalanx and the distal epiphysis of the first phalanx of the thumb. Case III.—Bifid fifth toe. The proximal phalanges of these twin toes were united at the base; each had a separate articulation with the head of the fifth metatarsal bone. Case IV.

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—Sixth toe on the left foot. The fifth metatarsal bone was bifid at its distal extremity, the two heads supporting the fifth and sixth toes. The axis of the right foot, in Case V., was constituted by the second metatarsal bone. The other bones had a tendency to spread out, which gave to the foot somewhat the appearance of a fin. The last phalanx of the great toe was dislocated externally; along the external border of the first metatarsal bone there were 3 fragments of a supplementary metatarsal bone, which had incompletely developed or had been partly resorbed.

The phylogenetic study of the development of the limbs has led to the following conception: the polydactyl extremity of fishes becomes the oligodactyl extremity of man through unilateral atrophy of most of the rays of the fins. These cases bring further support to the theory of the ichthyopsidian origin of the higher vertebrates.

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**An Unusual Case of Unilateral Supernumerary Thumb.**

*E. Francois-Dainville and M. Léonard, Bull Soc. anat. de Paris, 18:433, Oct.-Nov., 1921.*

An extra thumb was present on the right hand of a mentally defective man of 50. Death of the subject permitted removal and preservation of the anomalous hand. The extra digit is small and contains 2 diminutive phalanges, very well proportioned. The first metacarpal is one-third larger than the normal bone; 15 mm. from its distal end it divides, forming a fork. The rest of the shaft is single. The internal limb of the fork is larger and bears the articulatory surface (metacarpophalangeal) of the internal and larger thumb. The external branch bears the head which articulates with the first phalanx of the extra thumb. The 2 metacarpophalangeal articulations are entirely separate. In structure, the abnormal metacarpal suggests fusion of 2 bones. The case is thus distinctly different from bifid thumb due to an extra phalanx; and is also at variance with usual types of polydactilism in which (1) the abnormal thumb articulates, by its first phalanx, with a normal metacarpal, or (2) the first metacarpal, otherwise normal, bears an extra articular surface. The muscles and tendons have the following relations: The insertion of the flexor brevis is normal. The abductor brevis supplies fibers at the metacarpal fork to the metacarpophalangeal joint of the extra thumb. The adductor pollicis has a small, supplementary insertion on the external limb of the fork. The relation of the other muscles is normal. The tendon of the flexor longus divides at the bony fork. The dividing portion is inserted on the palmar aspect of the second phalanx just below the phalangophalangeal joint. This insertion is joined to the tendon of the extensor brevis by a strong, tendinous expansion. The tendon of the abductor longus is inserted a little above the base of the metacarpal, under its opponent. The extensor brevis is inserted on the first phalanx of the extra thumb and is united to the extra tendon of the flexor longus. There is a supplementary arterial branch from the superficial palmar arch which gives off 2 collaterals to the extra thumb. The palmar branch of the median

nerves gives off 2 collaterals, and external fibers from the radial nerve supply the back of the extra thumb. A diagram and drawing made from the radiographic plate are supplied.

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**Rigor Mortis.**

*Hans Winterstein, Pflüger's Arch. f. d. ges. Physiol., 191:184, Berlin, Oct. 24, 1921.*

Presumably rigor mortis depends on the accumulation of lactic acid, as neither this accumulation nor any contraction takes place with ample oxygen supply. Oxygen, however, prevents the accumulation of lactic acid, or transforms it into the original material. New experiments on the sartorius muscle in the frog showed distinct contraction, in a nitrogen or hydrogen atmosphere, in winter on the second day and after a few hours in summer. In boiled Ringer solution through which nitrogen or hydrogen is passed continuously, the contraction was absent, obviously because lactic acid was removed. The solution always contained lactic acid. Inasmuch as the removal of lactic acid prevents rigor mortis, the latter depends essentially on its accumulation.

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**Tissue Respiration in Inflammation.**

*H. Gessler, Arch. f. exper. Path. u. Pharmakol., 91:366, Leipzig, Nov. 22, 1921.*

Oxygen consumed is determined in excised tissue gasometrically by indirect calorimetry. Normal and inflamed pieces of skin are compared as regards oxygen consumed. The most suitable skin is that of the pig. Mustard oil spread externally had no characteristic action. Subcutaneous or intracutaneous injection of 0.1 to 0.2 gm. mustard oil, or 0.5 gm. formic acid produce inflammation followed by necrosis. The vicinity of the necrosed parts shows increase in oxygen consumed according to the intensity of the inflammation as against normal comparative pieces of skin. The increase in oxygen consumed (measured in respiration vessels connected with Barcroft manometers) depends on increased metabolism. As the proportion of fat in the skin has to be taken into consideration, the result is reduced to nitrogen content (Kjeldahl). The experiments were conducted at 37° C.

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**Experiments upon Immunity to Tumor Growth.**

*Helen Chambers, Gladwys M. Scott and S. Russ, Lancet, 202:212, London, Feb. 4, 1922.*

A considerable degree of immunity has often followed the inoculation of quite small pieces of irradiated tumor. In order to find how the degree of immunity varied with the amount of material, 80 rats were given quantities of irradiated Jensen's rat sarcoma ranging from 0.003 to 0.2 c.c. Fourteen days later all these animals and the controls received a test inoculation. The degree of immunity did not vary much. The best result was obtained with the largest quantity, and in subsequent tests 0.2 c.c.

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was used. The maximum effect was reached rapidly, as in other immunity reactions, and was lasting. Experiments were undertaken to determine whether the immunity produced by the absorption of irradiated tumor would have any effect on an established growth. Animals bearing single tumors were treated with tumor tissue which had been exposed, outside the body, to a lethal dose of radiation. There appeared to be a definite effect on the established tumor, for after the immunizing dose the tumor grew progressively in only 5 animals. Animals with 2 growing tumors were treated by exposing one tumor to a lethal dose of radiation, while the growth of the untreated tumor in the same animal was recorded. The treated tumors disappeared. A study of the influence of the condition of the tumor on its power to confer immunity showed that the rapidly growing tumor had much the greater effect. Only 5 rats out of 30 grew tumors; these animals were smaller than the majority of the controls. Experiments were undertaken to determine the effect of reducing the dose of radiation below the amount necessary to kill the growth cells. Twenty-eight normal rats were given inoculations of Jensen's rat sarcoma into each axilla, 35 control animals being inoculated at the same time in the left axilla only. Five days later when the tumors were palpable, those on the right side were exposed to the radium capsule for a time corresponding to a dose of  $\frac{1}{3}$  rad. Four weeks later the volumes of the irradiated tumors were much smaller than the controls, but the untreated tumors on the opposite sides of these animals were quite as large as the controls.

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**A New Transmissible Chicken Tumor.**

*Teutschlaender, Beiter. z. Path. Anat., etc., 69:489, Jena, Oct. 13, 1921.*

The tumor, which was described at the meeting of the German Pathological Society in Jena, had been taken from the lower part of the left side of the neck and the left breast of a hen about 1 year old. Histologically it was a spindle-cell sarcoma which had infiltrated the muscle-fibers and partly destroyed them. Metastases occurred in both lungs, in the heart and liver, and kidney, and in the parietal and visceral peritoneum. A small portion of the tumor was transplanted by means of a trocar into the right chest wall of another hen. This animal died on the one hundred and forty-third day; at the point of inoculation a malignant tumor of the same structure as the implanted portion (spindle-cell sarcoma) was found. Careful histologic examination showed that it was not a granuloma, but a true blastoma. Its malignant nature was demonstrated by its behavior toward neighboring tissues. Such a growth is a mixed-cell sarcoma, in part desmoplastic, or myxomatous, or angiomatous, and combines the features of the first tumor described by Rous with those of Jujinamo and Inamoto, and Rous' third tumor.

Transplantation from one animal to another succeeded both when portions of the tumor were used and when inoculation was made with cell-free material (filtrate inoculation), as well as when powdered tumor material was used.

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**Experimentally Produced Mouse Carcinomas Following Inoculation with Human Carcinoma and Sarcoma.**

*Fr. Keysser, Arch. f. klin. Chir., 117:319, Berlin, Nov. 17, 1921.*

The author has devised a new procedure for the inoculation of human tumors into mice: The original substance of the human tumor was irritated by Roentgen or radium rays, and the tumor cells were sensitized by previous treatment of the host with alien tumor extracts. Keysser was successful in inoculating 4 human tumors into mice. The mouse tumors, with the exception of one section, uniformly showed true tumors. It was not a matter of further growth of the human tumors, but of tumors originating from the tissues of the mice themselves.

It can be seen from these findings that histologic variations may appear in the primary tumors and the tumor metastases, in the sense that the borderline between carcinoma and sarcoma disappears. The duration of growth in the inoculated primary mouse tumors is much shorter (as is shown in a case reported). The slow growth of the inoculated human tumors remains approximately within the same limits, even with subsequent passages in the mice. The inoculation of spontaneous tumors into mice also produces a very slight result, which can be increased only in subsequent passages. This explains the same relationships in human material. How the inoculation of a malignant human tumor causes the development of a malignant mouse tumor cannot as yet be definitely explained. The accidental coincidence with spontaneous tumors of mice can, with slight exceptions, be definitely excluded. The probability that the inoculated human tumor tissue acts as a stimulant, by means of which malignant tumors arise at the site of the effect of autogenous tissue, is indeed very great, but is demonstrable only by means of further experiments. The former inoculation experiments of other authors possess no demonstrative power in this direction.

The author's experiments lead to the following conclusions: White mice are suitable for inoculation experiments with human tumors, provided the work is done aseptically. The selection and preliminary treatment of the original tumor render the inoculation successful. Only a small percentage of tumor formations occur in mice, which fact corresponds to the poor results of inoculation of spontaneous mouse tumors in mice. The duration of development of the inoculated tumors from human tumor tissue is considerably longer than with inoculated tumors derived from spontaneous mouse tumors. Only further experiments will show whether the inoculated human tumor tissue acts as a chemical stimulant, or with the aid of a specific excitant, or whether it is a matter of a transplantation of tumor cells, which undergo a change in the alien organism.

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**Production of Experimental Tar-Carcinoma.**

*B. Lipschütz, Wien. klin. Wchnschr., 34:613, Dec. 22, 1921.*

The author succeeded in producing tumors of the skin in 45% of mice (chiefly gray) which were painted with coal-tar. The tumors appeared in from eighty-eight to one hundred and twenty-five days. The tumors are like warts or papillomas and are sometimes pluricentral with a tendency to generalization. The latter feature is occasionally seen after subcutaneous inoculation of animals which were not painted with tar. The inoculation was made with the tar-carcinomas. One of these successful tumor transplants formed a subcutaneous tumor about the size of a cherry and of sarcomatous structure. There is a peculiar pigmentation of very dark color in the vicinity of the tumor. The same pigmentation occurred after implantation of small fragments of the warty tumor of animals which were subjected to tar. Transplants of this tumor in animals which were not subjected to tar also showed this pigmentation, thus proving that the pigmentation has nothing to do with the tarring. The author is unable to explain this pigmentation. He can only say that the pigment is autochthonous and melanotic, that it remains unchanged in substances which dissolve fats and is not altered by concentrated acids. It gives no iron or oxydase reaction and is bleached by prolonged action of  $H_2O_2$ . One of the animals with tumor also showed many nodules which resembled miliary tubercles, diffusely spread, yellow in color and as large as the head of a pin. These consist of areas of invasion of the epithelium into the upper layers of the corium with subsequent formation of cystic bodies.

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**A Peculiar Variety of Carcinoma Metastasis in the Pelvic Connective Tissue (Contribution to the Study of Dimorphous Carcinoma of the Cervix).**

*A. Seitz, Beitr. z. path. Anat., etc., 69:395, Jena, Oct. 13, 1921.*

During a radical operation for the extirpation of a cervical carcinoma, a neoplasm about the size of a small hen's egg was removed from the region between the right obturator nerve and the right lateral umbilical ligament. It proved to be a cyst lined with squamous epithelium, suggesting at first the diagnosis of epidermoid. Subsequent examination showed carcinomatous nests in the cyst wall, which corresponded histologically with the cervical tumor. They were made up of mature cells, arranged peripherally, and of centrally located immature cells. Hence the tumor is a dimorphous carcinoma, which acquired a cystic form when the immature cells underwent necrosis.

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**Cylindromas.**

*George Herzog, Beitr. z. path. Anat., etc., 69:422, Jena, Oct. 13, 1921.*

Report on a case of cylindroma of the orbit in a male patient 46 years of age, with extensive destruction of the bones of the

skull, and metastases in both lungs. Histologically, several formations were found: gland-like cell tubules, tiny cysts, or solid cell cylinders, and between them a net-work of hyaline connective tissue structures. In some regions this preponderated over the finger-like epithelial cell growths; elsewhere the epithelial proliferation predominates and the hyaline connective tissue may be absent. Occasionally the picture simulates that of myxosarcoma. The solid cell cylinders are the most recent formations in this new growth characterized by hyaline connective tissue and cavities. The hyaline structures which have formed in epithelial spaces, or at the periphery of the cellular proliferations, are to be regarded as epithelial elimination products. Connective tissue enters the cavities; its fibers unite with the original contents to form a solid hyaline mass, that is, the hyaline structures have a double origin. In the present case the tumor springs from a glandular organ, probably from the glandular appendages of the ethmoidal cells. In 3 other cases the formation of gland lumina could be demonstrated, and in 5 cases of basal-cell carcinoma of the facial epidermis such lumina or their casts could be demonstrated.

Herzog is inclined to regard the cylindroid formation of these tumors to be a tumorous growth of the membrana propria. He reviews the literature on the derivation of cylindromes from endothelioma of blood-vessels and lymph-vessels, or from endothelial structures. He recognizes in them epithelial tumors which are characterized by the formation of peculiar cavities, with solid contents. The production of a homogeneous epithelial secretion, and its special action on connective tissue, form a connecting link between cylindromas and other epithelial tumors, such as certain adenomas of the mammary gland and of the prostate. Possibly, also, there is a relation between scirrhouss carcinoma and cylindroma (epithelioma cylindrosom). The latter name is to be retained.

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**Ganglioneuroma Xanthematosum.**

*H. Beitzke, Beitr. z. path. Anat., etc., 69:400, Jena, Oct. 13, 1921.*

Autopsy on a man 57 years of age revealed, besides general arteriosclerosis, a tumor in the angle between the pons and the left cerebellum. Histologically, it was shown to be a neurinoma, which, however, contained numerous triangular or pyriform cells, diagnosed as ganglion-cells. Extremely large, round cells, filled with doubly refractive material—xanthoma cells—were also found. Neither regressive nor resorptive processes can explain their presence. They must be regarded as the result of an active process, or as true xanthoma cells. Apparently, an excess of cholesterol in the blood, and the existence of well-vascularized tumors, furnish conditions which favor the deposition of cholesterol and the genesis of xanthoma cells in tumors.

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**Albumin Crystals in the Uriniferous Tubules in Cases of Multiple Myeloma.**

*M. Loehlein, Beitr. z. path. Anat., 69:295, Jena, Oct. 13, 1921.*

In a case of multiple myeloma, in which Bence-Jones albumin had been demonstrated in the urine during life, the cortical canals in the kidneys were greatly dilated and contained crystalline accumulations. Crystalline casts were found in most of the tubules of the marrow and of the collecting tubules. They were surrounded by masses of polymorphonuclear leukocytes and giant-cells. Microscopical and microchemical examination indicated that it was crystalline albumin, probably Bence-Jones albumin crystals.

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**So-Called Syringoma.**

*L. Arzt, Beitr. z. path. Anat., etc., 69:408, Jena, Oct. 13, 1921.*

Report of 4 cases which showed multiple small dense brown or brownish-red nodules in the skin, especially in that of the chest. Histologically, these nodules consist partly of solid islands of cells, partly of cystic cavities lined with epithelium. The derivation of these cells (from endothelium or epithelium) is attributed to an epithelial genesis. The author believes with Quinquand that epithelial cells of the epidermis, which have been cut off during embryonal life, are the cause of these small tumors. The cystic cavities result from a degeneration of the solid islands. The author proposes the name of "benign cystic epithelioma of the type of syringoma."

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**The Biologic Reactions of Tissue Extracts (Cytosts) in the Production of Acute and Chronic Diseases.**

*Fenton B. Turck, Bull. Acad. de méd., 87:31, Paris, Jan. 10, 1922.*

Experiments have shown that when the thigh of a dog is crushed and several hours later an emulsion of the disintegrated tissues is injected to another animal, fatal symptoms of shock are produced in the latter. If the crushed thigh of the dog is ligated at the time of the injury and the ligature removed after several hours, the animal also dies with symptoms of shock as a result of the absorption of disintegrated albumins. In all animals dying under these conditions an intense stasis of the circulation is noted in the splanchnic zone. In another series of experiments produced were localized autolyses through the repeated injection in the same place of chloroform, ether or alcohol. In this way more chronic or attenuated forms of shock were induced in these animals. At autopsy congestion of the lungs, liver and intestine was found and also foci of pulmonary necrosis, of coagulation necrosis in the liver and erosions of the pylorus and duodenum, similar to peptic ulcers. It is claimed by Turck that certain mechanical, physical or chemical traumas, of a less violent nature than those mentioned, may liberate from the cell a substance which is loosely combined with it. This substance may be isolated; it has been found in protozoa and in the cells of animals and vegetables. To this the name of cytost is given. In weak concentration it excites

metabolism and cellular segmentation. In higher concentrations it causes an excessive viscosity reaction and slows down metabolism. At a still higher concentration it produces such a degree of viscosity that death ensues (through shock). There is in the cells and in the blood an antagonistic substance known as anticytost. The plasma of vigorous adult animals contains an excess of anticytost, so that when cells are placed in the plasma of these animals their metabolism and segmentation is inhibited. This inhibiting action may be neutralized by the addition to the plasma of a small quantity of cytost. Conversely, when a normal culture of tissues begins to die, owing to an excess of cytost, the addition of anticytost revives it.

Animals may be actively immunized against lethal doses of cytost. Injections of moderate doses of cytost in old cats produced a marked increase of weight, but not of fat. The coat of the animals became silky, their muscles hardened and they became playful. Administration of too high doses, on the other hand, caused disturbances of metabolism, arteriosclerosis, nephritis, gastric ulcer, and general emaciation. Anticytost serums may be obtained by inoculating animals with cytost, but these are effective only for the animal species from which the cytost was obtained. Human anticytost serum can be obtained by injecting increasing doses of human tissue extracts in horses.

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**The Pathologic Anatomy and Pathogenesis of Diseases Due to Undernourishment and Exhaustion.**

*Lubarsch, Beitr. z. path. Anat., etc., 69:242, Jena, Oct. 13, 1921.*

The author has elsewhere described the condition of the organs in diseases due to exhaustion, recording 10 cases of simple exhaustion and 46 of exhaustion combined with other maladies. In the present publication he emphasizes the marked diminution of fatty and lipoid substances, as well as the destruction of red blood-cells, with its consequences, and the repeated and continuous hemorrhages in the connective tissue. Extensive injury of the walls of the capillaries is an important factor in the production of edema. Contrary to the view of Prym, the author maintains that starvation edema belongs in the class with scurvy. Moreover, close relations probably exist between it and starvation osteopathy; edema was frequently observed during the course of the latter disease. Unfortunately, no examination of the bones was made in edema. Apparently no sharp distinction can be drawn between cachexias due to undernourishment, and avitaminoses.

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**An Almost Complete Bilateral Necrosis of the Renal Cortex in Diphtheria.**

*W. Stockenius, Beitr. z. path. Anat., etc., 69:373, Jena, Oct. 13, 1921.*

In a patient 46 years old, who died of severe pharyngeal and laryngeal diphtheria, the greater part of the cortex in both kidneys was necrotic. Many large vessels (interlobular arteries) were thrombosed and revealed hyaline degeneration almost from their point of origin at the arciform artery to their termination at the glomerular loops.

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**Pathologic Anatomy of Foot-and-Mouth Disease.**

*E. Emmerich, Beitr. z. path. Anat., etc., 69:103, Jena, Oct. 13, 1921.*

Examination of the divers organs of calves, cattle and pigs yielded in part the well-known changes. The resemblance to small-pox is striking in the lesions of skin and mucous membranes. In cases ending fatally, the heart was invariably greatly affected, there being marked parenchymatous degeneration, and in other cases severe inflammation. The latter was especially frequent in cattle, so that the sudden demise in foot-and-mouth-disease is to be regarded as cardiac death. There is reason to believe that animals which survive an attack of foot-and-mouth-disease usually sustain severe cardiac injuries. No changes have been found in the brain.

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**Postmortem Findings in Twelve Cases of Plague.**

*Henry Hartman and Anna Bowie, J. A. M. A., 78:493, Feb. 18, 1922.*

Eleven of the cases of plague were of the bubonic and one of the pneumonic type, which occurred during the recent outbreak of the disease in Galveston. The first intimation of the presence of plague was the discovery of a human case in this city. The disease was diagnosed clinically and confirmed by bacteriologic examination and by the typical findings at necropsy. From that time, necropsies were held on the bodies of all patients dying in the hospital or city, when the cause of death was suspicious. In this series there were 6 males and 6 females. External examination of the body revealed as the most prominent change the presence of a swelling of one or more groups of the more superficial lymph nodes, one of which represented the primary localization of the disease. In Case 10 there were no enlarged glands and there would have been failure in diagnosis if the gross findings had been depended upon solely. The axillary glands on both sides were enlarged in the second necropsy of the series, and the cervical glands in Case 9. In the other 9 necropsies, the primary localization of the disease was in the femoral chain of the superficial subinguinal glands. In addition to the duskiness over the indurated area at the site of the buboes, small hemorrhages were present in the face and side of the neck in Case 12; muscular eruption of the arms and hands in 4 instances, and of the chest in 3 of these. A rather large bleb was present in Case 3 over the site of the bubo. Of the 5 patients showing petechiae, none received serum; so the petechiae cannot be explained as anaphylactic in origin. Among other necropsy findings were metastatic areas in the liver, hemorrhage in the pancreas and in the sinus of the kidney.

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**Liver Findings in Guinea-Pigs Suffering from Typhus Fever.**

*Max H. Kuczynski, Klin. Wchnschr., 1:8, Berlin, Jan. 1, 1922.*

The author reports the findings in guinea-pigs infected with tissue cultures of animals diseased with typhus fever. The findings resemble those in the liver of a man with typhus fever and recently reported by

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the author. He described groups of very small globules in the endothelial cells. These globules resemble the Rickettsia bodies in the intestine of the louse. Endothelial stimulation and proliferation were described in the spleen and liver of persons with typhus fever, as were disintegration and phagocytosis of the red and white corpuscles, non-mobilized and free macrophages and leukocytic hyperregeneration. The same typical changes are to be attained in experimental infection of guinea-pigs. There are found stimulation of the liver endothelium, phagocytosis, change of cells to basophils and cells which resemble plasma cells, which are free and may be seen in the peripheral circulation. Local accumulation of finely granular virus could be seen within greatly enlarged endothelial cells. There were various sizes and stages of development. The endothelial cells may burst and allow the contents to escape. It is possible to show the similarity to the parasites in the intestine of the louse. The cells do not usually perish. The endothelium is apparently a physiologic medium for the development of the virus.

The conditions of the virus in man and the guinea-pig, with the extensive cellular reaction and pouring out in the circulation, explain the character of the fever which is missed in rabbits, because this animal harbors but little of the virus. Serum from convalescents protects man and the guinea-pig but not the rabbit. The search as to the possibilities for reinfection may reveal that there is a purely cellular immunity for one kind of infectious agent and a humoral immunity for another. The author points to the similarity of his pictures of the virus cells with chlamydozoa. It is possible that the unity of the change of the cells in the host which are infected with the cellular parasite is an expression of a common condition for life. This may be substantiated by the similar picture of the cells of the various forms of the virus.

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**Primary Aleukemic Splenomegaly.**

*R. Josselin de Jong, Beitr. z. path. Anat., etc., 69:185, Jena, Oct. 13, 1921.*

Histologic examination of aleukemic splenomegaly shows the necessity of sharply separating the follicles from the pulp. Proliferation of the follicles produces only lymphoid tissue, i. e., we are dealing with lymphadenoses of uniform character. Proliferations of the spleen pulp, owing to the variation of the histologic structure, may produce various formations. The author suggests for these latter lesions the name pulposis, of which there are several varieties—a pulposis of Gaucher's type, a fibrous pulposis of Banti's type, and a hyperplastic mixtacellular pulposis. Further research is needed to decide whether a myeloid, a reticulo-endothelial or a fibro-endothelial type of pulposis occurs.

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**Periarteritis Nodosa in the Pig.**

*E. Jost and Harzer, Beitr. z. path. Anat., etc., 69:85, Jena, Oct. 13, 1921.*

Report on 2 pigs, showing periarteritis nodosa. The alterations in the vessel walls correspond in every particular to the same lesion in man, especially in regard to pathologic changes in the elastic coat, hemorrhages and necrosis of the vessel wall, the production of false aneurysms, thrombosis or obliteration of the lumen, and disease of the adventitia and surrounding tissues. Histologic examinations seem to point to the adventitia, not the intima, as the primary focus. No indication is given of the etiology of the pathologic process.

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**The Nature of Leukocyte Inclusions in Lethargic Encephalitis.**

*Ugo Pardi, Cntrlbl. f. Bakteriol., etc., 87:406, Jena, Dec. 30, 1921.*

Hilgermann, Luxen and Shaw have reported bacteriologic and clinical findings in encephalitis lethargica, in which they succeeded in demonstrating special structures in the dark field and also in blood-smears stained with Giemsa's stain, and in liver punctates. They believe that these structures are the cause of the disease.

However, Pardi states that these structures are the same as those found by Döhle in 1912, in the blood of scarlet-fever patients, and assumes that they are not specific. They are to be regarded rather as degenerations of the plasma of neutrophil polymorphonuclear leukocytes which may be produced by the action of various toxins. They may also be produced experimentally by the use of various infections and toxic irritants.

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**Tuberose Sclerosis and Tumor.**

*K. Berliner, Beitr. z. path. Anat., etc., 69:381, Jena, Oct. 13, 1921.*

In a man 25 years of age, who during life had manifested the signs of a cerebral tumor and had presented a sebaceous adenoma of the cheek and forehead, examination of the brain revealed the lesions of tuberose sclerosis. The tumor presented the picture of a cylindroma, a new growth related to the peritheliomas; this seems to support the view which some authors hold concerning the nature of tuberose sclerosis.

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**Heterologous Cell Structures in Goiter.**

*Ludwig Merk, Mitteil. a. d. Grenzgeb. d. Med. u. Chir., 34:554, no. 4, Jena, 1922.*

If the vesicles in a freshly removed goiter are opened, the contents sucked up in a capillary tube and placed under the microscope, spores are almost always found; in the bladder walls there are often yellow or rust-brown bodies which also contain large numbers of spores. The spores are bodies about 5 microns long, similar in their yellow coloring to red blood-cells, but differing from them in their marked refracting capacity. They have the form of a many-sided pyramid, the base of which shows a depression. They are not cap-

able of independent change of location, but show a movement similar to brownian molecular movement. The spores consist of a glassy, transparent and a strongly light-refracting portion, and stain with safranin, methyl-green, peronin and hematoxylin.

On picking fresh goiter tissue to pieces one can see with the naked eye yellowish-brown structures which contain spores. The author calls these structures spore sacs. There are also cells in the fluid from goiters which, because of their yellow color and the rust-brown clumps in which they appear, Merk calls rust cells. They can be seen with the naked eye as small bodies resembling gravel embedded in a transparent gelatin; they are round or egg-shaped, and generally about 30 microns long. They contain a vesicular nucleus, clear as glass, varying numbers of strongly refracting bodies, and rust-brown spheres. The rat cells are surrounded by a plasmatic border which refracts light only slightly. Much more rarely the author found in goiters large egg-shaped cells with a smooth, shining cell membrane supplied with numerous granules of a bright yellow color, between which was an extremely small nucleus. The author thinks that the spores are not vegetable cells. The egg-shaped cells are certainly animal, as are probably the rust cells also. He thinks that all 3 forms are animal cells of the same species, probably a protozoön.

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**Myxedema.**

*Ceelen, Beitr. z. path. Anat., etc., 69:342, Jena, Oct. 13, 1921.*

In a woman 57 years of age, a typical myxedema was found. The thyroid gland was greatly reduced in size; its histologic structure almost unrecognizable. Only meager traces of parenchyma remained; the rest of the gland consisted of epithelial bars and nests in dense connective tissue, giving a picture resembling that of scirrhous carcinoma. Chemical analysis revealed total absence of iodin, and showed the amount of adrenalin in the suprarenal capsules to be barely one-third of the normal.

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**The Pathologic Anatomy of the Suprarenal Capsule.**

*Huebschmann, Beitr. z. path. Anat., etc., 60:352, Jena, Oct. 13, 1921.*

Report of a case of Addison's disease, in which there was an atrophy of both suprarenals, and of a case of mitral lesion accompanied by atrophy of the right and moderate hypertrophy of the left suprarenal. In this second case the atrophy of one suprarenal gland was due to syphilis; the same was suspected in the first case (aortic changes), but the Wassermann test was negative. The author invites discussion of the question whether a deep-seated primary injury is not the more important factor. In that case, atrophy would be the final stage in the disease process, comparable to liver cirrhosis following acute yellow atrophy. A true compensating hypertrophy of the adrenal does occur, the cortex being the vicarious portion. Cortex and marrow are to be considered separately; the former is the more important part of the organ.

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**The Alterations of the Cover Cells of the Peritoneum.**

*Felix Marchand, Beitr. z. path. Anat., etc., 69:1, Jena, Oct. 13, 1921.*

The author includes a detailed account of prior research. There were notes, specimens and drawings of 17 experiments during which guinea-pigs were injected intraperitoneally with increasing amounts of emulsions of lycopodium (1.5-4 c.c.); the duration of the experiments varied between four hours and nine days. Accurate histologic examinations show that sterile lycopodium grains, introduced into the peritoneum, are fixed to the peritoneum by fibrin, within a few hours. The first step is the migration of polymorphonuclear leukocytes; then follows an accumulation of mononuclear cells. Very soon changes appear in the cover cells of the peritoneum. These cells originate in the epithelial mesoderm, and may therefore be designated as true epithelium, although they retain close relations with the mesenchymatous cells. Today, the term "epithelium" has a morphologic significance only, and requires, for further distinction, the particular genetic epithet.

In the present experiments it could be demonstrated by direct examination of fresh material on the warm examining table, as well as in sections, that the cover cells change into contractile, vacuolated structures which separate from the substratum. Their mass is augmented by pus. They form round or polygonal, stellate or spindle-shaped elements in various positions, which attach themselves to the foreign bodies (lycopodium grains) and may become contractile giant-cells by direct nuclear division. The spindle-shaped and filiform fiber cells fix the foreign body to the trabeculae by means of connective tissue stems. After they have completely enclosed the foreign body the cover cells again assume epithelial forms. The motile descendants of the cover cells present active phagocytosis and thus form a part of the macrophages. The genesis of large and small lymphocytes from the cover cells has not been demonstrated.

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**A Pendulous Cavernous Lymphangioma of the Exterior Gastric Wall.**

*S. Oberndorfer, Beitr. z. path. Anat., etc., 69:418, Jena, Oct. 13, 1921.*

The tumor was discovered at autopsy in a young man 19 years old who had died of peritonitis following tonsillitis. It was as large as the palm of the hand, was attached to the lesser curvature by a pedicle, and lay across the sinus and the pyloric canal. Histologically it was an actively proliferating cavernous lymphangioma with endothelial proliferations, and had its origin in aberrant lymphatics of the small omentum. It probably produced no clinical symptoms.

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**The Occurrence of Ciliated Epithelium in Gastric Carcinoma.**

*U. Quensel, Beitr. z. path. Anat., etc., 69:474, Jena, Oct. 13, 1921.*

Among 137 cases of gastric carcinoma the author found epithelium with ciliated or cuticle margin in the case of 46 patients. In

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26 out of these 46 they were found only in isolated preparations of the carcinomatous juice, and (in 17 cases) in very small numbers only. In 16 cases the ciliated cells were also found in sections; 4 cases had been examined histologically only, with positive results. The author found similar cells in 2 cases of carcinoma of the bile-ducts, and in the pleural exudate in a case of pulmonary carcinoma. He interprets the occurrence of these ciliated cells as a metaplastic phenomenon due to local conditions.

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**A Dysontogenetic Tumor of the Ureter.**

*A. Binder, Beitr. z. path. Anat., etc., 69:462, Jena, Oct. 13, 1921.*

Patient, a woman of 68 years of age, died of cerebral hemorrhage due to marked arteriosclerosis. At autopsy, the lower end of the left ureter was found to consist of a coarse cylindrical tumor which extended into the bladder and caused the epithelium to project. Its surface presented flattened nodules. Histologically, it was composed of the normal cells of the ureter-transitional epithelium like that of the efferent tubules, connective tissue, and smooth muscle-fibre. The extent and the mutual relations of these tissues were such as to permit one to speak of a faulty mixture of normal tissue, and to designate the growth as a hamartoma or hematoblastoma. At the same time, uterine myomas were found.

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**Intestinal Emphysema in the Pig, and a Similar Lesion of the Urinary Bladder.**

*Olt, Beitr. z. path. Anat., etc., 69:549, Jena, Oct. 13, 1921.*

Report of a case of emphysema of the urinary bladder and 2 cases of intestinal emphysema in pigs. Culturally a colon bacillus of the non-motile *B. aerogenes* group was isolated; this was considered the cause of the lesion. The gas cysts of the bladder were found chiefly in the blood-vessel papillas; giant cells were also found in this locality.

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**The Healthy and the Diseased Pancreas.**

*R. Roessle, Beitr. z. path. Anat., etc., 69:163, Jena, Oct. 13, 1921.*

As yet we have no proof that any relation exists between the size of an organ and its working capacity. This is especially true of glands. To decide the question, it is first necessary to establish the anatomic conditions under different circumstances. The average weight of the pancreas is 88 gm.; the liver has about 19 times this weight. The relation to the total body weight remains fairly even during life; so also does the specific gravity (1.040). The pancreas grows steadily with the increase in the length of the body, and reaches its maximum size between the ages of 25 and 30 years. This it maintains into the forties. There is hypertrophy of the pancreas, which causes this organ alone to appear enlarged; its origin and significance are still unexplained. The author reports the following unusual findings: (1) In the case of a boy 12 years of age, with slight cirrhosis of the liver, there was marked fatty degeneration of the pancreas, with almost complete atrophy of glandular tissue. It could not be ascertained

whether or not diabetes had existed. (2) Numerous old and recent infarctions of the pancreas, histologically coagulation neuroses, analogous to anemic infarction of the kidneys were found. In the same case there was a focal, interstitial pancreatitis, and marked arteriosclerosis of the large and small vessels. (3) In the case of a woman 37 years old, suffering from obesity, a cyst of the pancreas was found, containing whitish tallow masses about the size of a hazelnut (like the contents of dermoid cysts). The cyst had suppurated and ruptured into the pleural cavity. (4) In a man 43 years of age a large round cell sarcoma of the pancreas existed, with numerous metastases in the nerves.

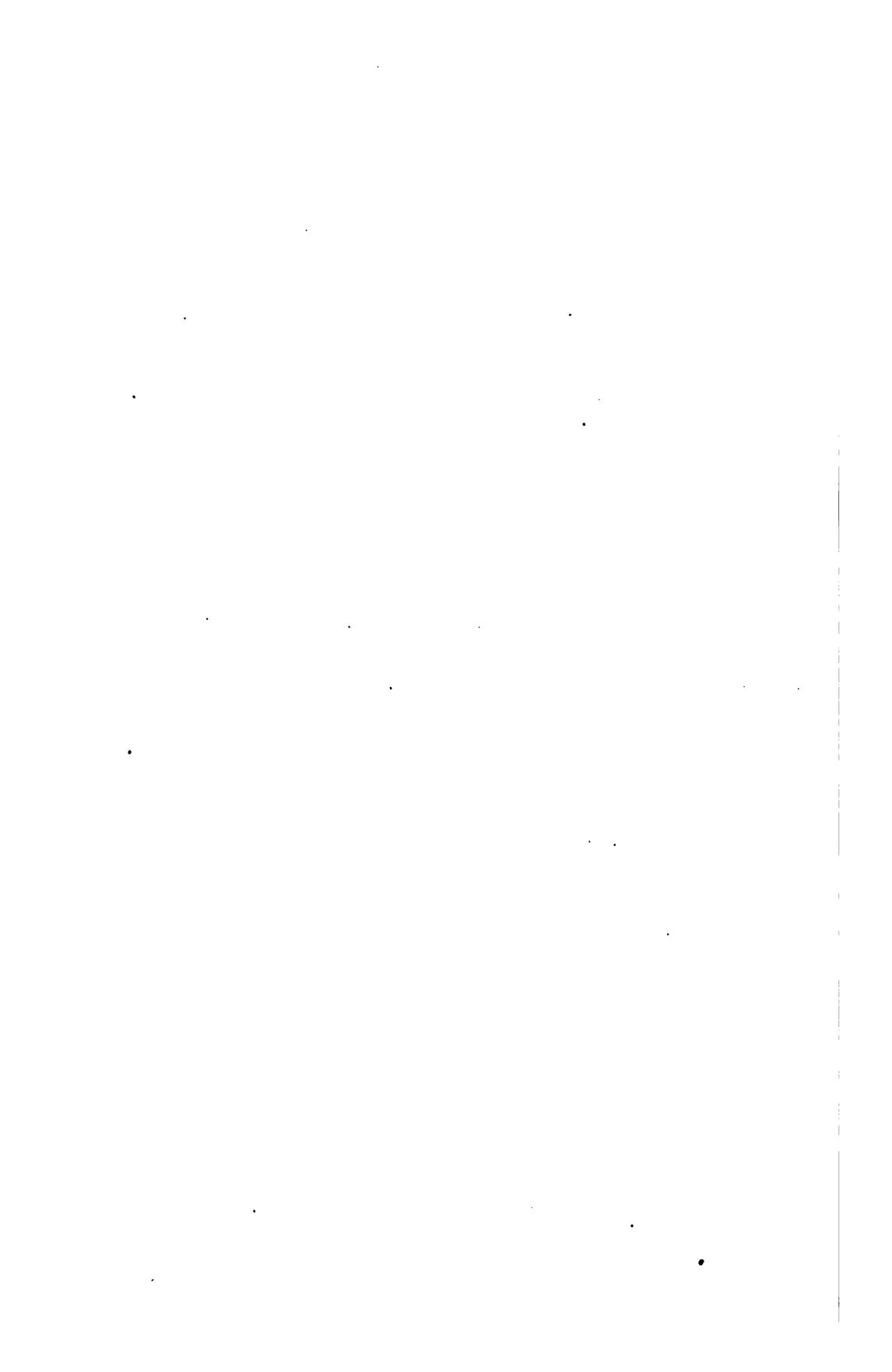
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**Epidermoid Cyst of the Pelvic Connective Tissue.**

*W. Siegel, Beitr. z. path. Anat., etc., 69:398, Jena, Oct. 13, 1921.*

In a woman 49 years old, palpation revealed a cystic tumor with a diameter of 7 by 5 by 4 cm. It was situated behind the rectum, at the level of the middle third of the vagina. Its wall consisted of connective tissue, with several layers of squamous epithelium. The author declines the diagnosis of dermoid or vaginal cyst, and considers it an epidermoid, the result of embryonic misplacement, at the border of the caudal intestine and neurenteric canal.

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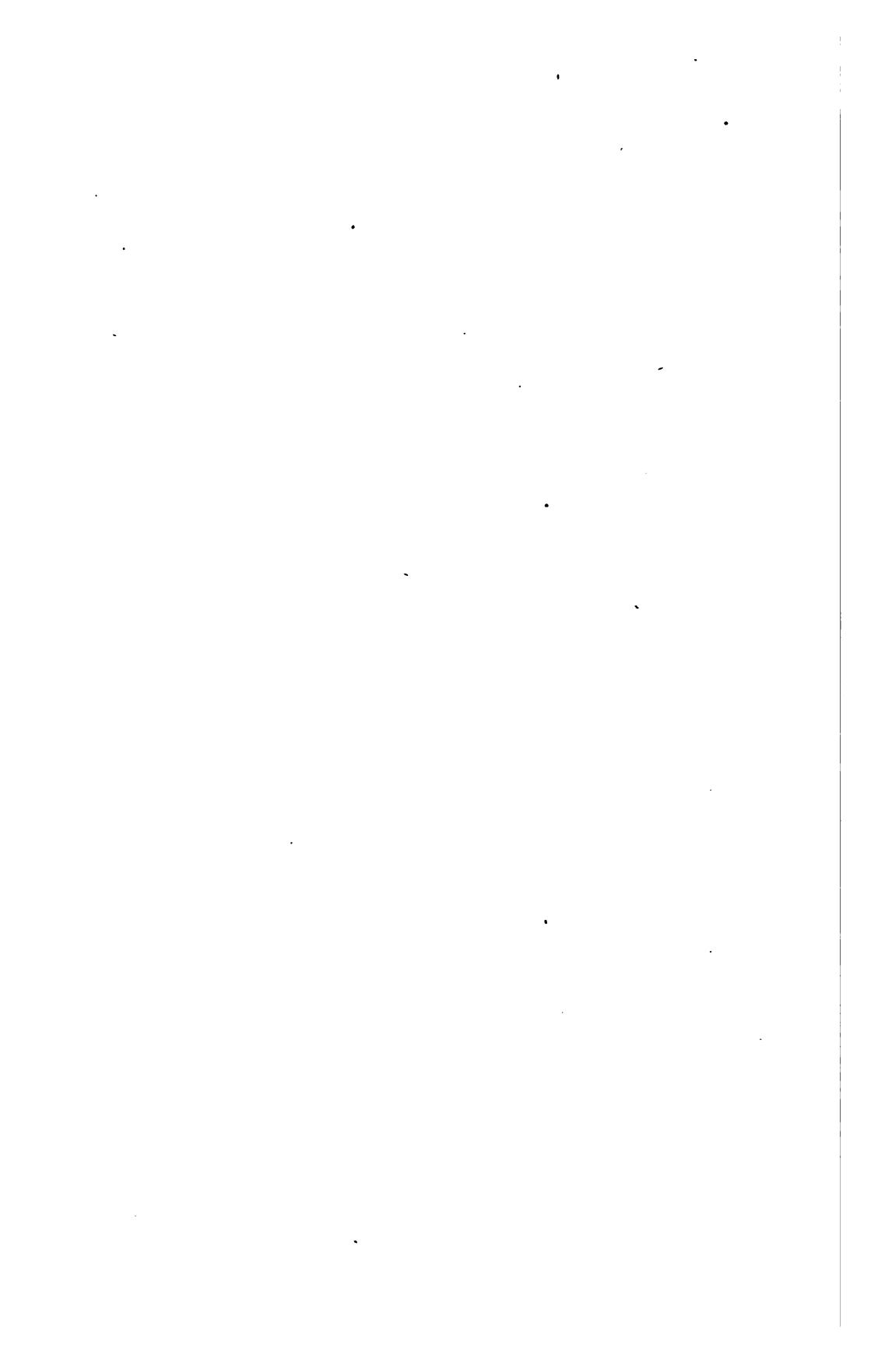
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**SECTION 1. ANATOMY, PHYSIOLOGY AND PATHOLOGY**

**1a. ANATOMY AND PHYSIOLOGY**

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**Studies of the Norm.**

*J. Kaup, Münch. med. Wchnschr., 69:189, Feb. 10, 1922.*

In a critical discussion of the 2 most important works on the norm in recent years, "Allgemeinen Prognostik als Lehre von der ärztlichen Beurteilung des gesunden und kranken Menschen" by Th. Brugsch, and "Untersuchungen über die Norm" by H. Rautman, Kaup says that the solution of the problem of finding foundations for the conception of the norm or normal type in measurement, number and weight is only possible by the united work of anthropologists, hygienists and clinicians. The measuring of variability with an average value and standard variation as a parameter, as suggested by Johannsen, compared with Gauss' probability curve is sufficient for judging a series of variations. Taking the average value as the typical value of a series of variations, the breadth of the normal should be determined by Martius' method. The boundaries of the normal and the pathological should be determined by observations of clinicians made in a uniform manner, and can be given in units of variation by addition to or subtraction from the average values. Rautman's studies are very significant for the most important bodily characteristics, and also as a basis for further investigation.

The new law of bodily proportions seems to be of increasing importance as a foundation for the judgment of the morphological and physiological correlation of the most important bodily characteristics. The clearing up of the correlative length and breadth of individuals of all sizes and the establishment thereby of possible correlations of all other morphological characteristics, such as the close relationship between metabolism, size of the heart, and activity of the heart, justify the expectation that there will be a still further elucidation of the relationship between the external and internal organization of the body. The parallelism between psychic and physical constitution is also given further support by this law.

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**The Arris and Gale Lecture on the Nerve Supply of the Parietal Peritoneum and Subperitoneal Tissues.**

*V. Zachary Cope, Lancet, 202:415, London, March 4, 1922.*

On clinical and embryologic grounds there can be no doubt that the diaphragmatic peritoneum is supplied with fibers from the phrenic. The same nerve also supplies the peritoneum covering the vena cava at the posterior border of Winslow's foramen. Similarly, the peritoneum and subperitoneal tissues of the anterior and lateral abdominal wall are supplied by the lower 7 thoracic and the first lumbar (iliohypogastric and ilio-inguinal) nerves. In the area of the quadratus lumborum and iliopsoas it is almost impossible to distinguish between the afferent

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nerves supplying the superficial fibers of the muscle (lumbar 1 and 2) and the tissues over the muscle. The twelfth dorsal supplies part of the tissues over the quadratus, and the first lumbar the area over the iliacus. In the central area of the posterior abdominal wall few afferent parietal nerves are to be found, and it is extremely difficult to ascertain the origin of these few. It is believed that the parietal peritoneum between the ascending colon and the mesenteric attachment is derived mainly from the right tenth and eleventh dorsal nerves, while between the descending colon and the median line the right twelfth dorsal nerve sends fibers. The parietal lining of the pelvis is probably derived from the fourth and fifth lumbar and the sacral nerves. In the renal region there are more nerves in the connective tissue behind the kidneys than in the peritoneum anterior to these viscera.

The clinical application of our knowledge of the nerve supply of the parietal peritoneum depends upon the different ways in which irritation of the nerve-endings may be manifested. Such irritation may be evidenced by: (1) local pain and sensitiveness; (2) referred pain; (3) hyperesthesia; (4) hyperalgesia; (5) muscular rigidity; (6) alteration of muscular reflexes. The manifestations depend partly upon the nature of the irritant. Normal parietal peritoneum is almost insensitive to touch, although the underlying tissues exhibit a greater degree of insensibility. Clear noninfective and nontoxic fluids do not cause any irritation other than the mere mechanical effect of the pressure or of the sudden flooding. Quite different is the effect on the coelomic lining tissues of the acrid and acid fluid which pours from a perforation of the stomach, or which collects in response to bacterial irritation. In such cases the peritoneum becomes congested, and the subperitoneal tissues swell with edematous fluid. Even when bacteria are the cause of the irritation the response is capricious, variable, and dependent upon factors not easily estimated.

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**A Silver Diffusion Method for Staining Nerve-Fibers in Paraffin Sections.**

*Walter Freeman, Arch. Neurol. & Psychiat., 7:321, March, 1922.*

The method described differs little from that of Warthin and Starry for the demonstration of spirochetes in paraffin sections. The only change has been the substitution of a gelatin film for the capillary space between the two cover-slips. One difficulty with the Warthin-Starry cover-slip method was the uneven character of the silver deposit. This was avoided by embedding the cover-slip, face up, in a warm 10% gelatin solution, allowing it to harden, and then pouring silver nitrate on the surface; the former then diffused down to the section. Later the gelatin was melted off and the cover-slip immediately immersed in the developing solution as recommended by Warthin-Starry. Even staining, so much desired in all silver preparations, was usually obtained.

This method, however, is not adapted to anatomic work, because it does not stain the finest ramifications of the nerve fibers, nor such fibers as are found in the deeper layers of the retina. Owing to shrinkage, the finest pericellular networks can only be brought out in very

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perfect preparations. It has advantages over the Bielschowsky frozen-section method in that larger sections are used, even the entire cross-section of the pons; the tissues are sectioned thinner, and the anatomic relations are maintained. The neurofibrils when not diseased, are well shown. Another advantage is that twin preparations can be made with consecutive sections, the one showing the cell processes and neurofibrils outlined in silver, and the other showing the identical cells stained by Nissl's method to show the tigroid bodies.

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### Hueck's Views on the Mesenchyma.

*Heinz Zimmermann, Virchow's Arch. f. path. Anat., etc., 236:29, Berlin, Jan. 14, 1922.*

According to Hueck the embryonal mesenchyma is a syncytium without individual cells and separate intercellular substance, and has at this stage no matrix or fibrils; these develop only secondarily, through differentiation. Matrix and fibrils are thus not amorphous structures, but have an independent power of development without the aid of cellular elements. This is further demonstrated in the adult organism during growth and regeneration. The matrix is therefore alive; hence life is not limited to the cell, and the cell is not the exclusive and elementary life-endowed structure. The author delves into the question whether, judging from the growth, differentiation, and regeneration phenomena observed in the matrix and fibrils, one may conclude that these structures lead an independent existence. He favors the adoption of such a conclusion. His exposition of the conception of the cell, as deduced from his teachings as to the origin of mesenchyma, does not destroy the validity of Virchow's views on cellular pathology, although the author's views represent one step beyond Virchow's theory.

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### Development of Articulations.

*Giulio Faldini, Chir. d. org. di movimento, 5:609, Bologna, Dec., 1921.*

Articulations are developed from the mesenchymal tissues which constitute the blastema of the joint. Very early the cartilage of the joints differentiates itself. The tissue constituting the intermediate disk is separated from the surrounding tissue by a connective lamina which differentiates itself from the primitive blastema. After the formation of the articular capsule, the external and internal ligaments of certain articulations differentiate themselves from the intermediate disk. The round ligament in the hip-joint seems to have its origin outside the first acetabular cavity of the tissue surrounding the glenoid fossa. The period of differentiation in the various articulations does not seem to be the same for all, nor does the differentiation take place from the proximal to the distal segment. The first articulations formed are those which are normally flexed by the habitual posture of the fetus. The differentiation of each articulation is always preceded by the differentiation of the muscular group which controls its mechanism. The formation of the articular cavity is almost contemporaneous with the

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differentiation of the articulation itself. In this formation there are noted arrests in development evidenced by adherence between the parts composing the articulation, which disappear only in a very advanced period of embryonal life. This fact is related to the development of the muscular system, since the adherence does not cease until complete movement of the articulation is made possible by the definite differentiation of all the groups and of the tendons which convey the motor energy to the given segment of the skeleton. The formation of the articular cavity occurs through the differentiation of the embryonal connective tissue and by mechanical displacement, without producing degenerative or liquefactive factors in the cells of the intermediate disk. In some articulations, the cavity, in the beginning of its formation, is all one, but in others, is divided by walls into several fissures which, becoming reduced and in part disappearing, give way, at the time of complete development, to a single cavity. Certain portions, free from the intermediate disk and from the septa which at first divide the articular cavity into compartments, according to whether we are treating with articulations which in their first stages are unilocular or multilocular, later becoming differentiated, give rise to synovial membranes. Vessels, which in certain articulations are particularly abundant, penetrate quite early. The cellular lining which covers the internal surface of the capsules and the articular ends is a differentiation of the connective tissue which assumes the form and disposition noted as a result of mechanical action. The development of articulations in general should be considered as owing to phylogenetic factors in the earliest stages of differentiation; related on the other hand to mechanical factors in later stages, and intimately connected with the muscular apparatus. This development repeats in its fundamental characteristics secondary histogenesis and morphogenesis.

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**The Development of the Anterior Lymphatics and Lymph Hearts in Anuran Embryos.**

*Otto F. Kampmeier, Am. J. Anat., 30:61, Jan. 15, 1922.*

The primary lymph sinus begins in approximately 5-mm. embryos of *Bufo vulgaris* in the form of small discontinuous anlagen. The originally solid lymphatic anlagen acquire lumina which have their inception as small crevice-like spaces in the cytoplasm between the large yolk globules. By continued proliferation and growth, the individual anlagen increase in length, bud collateral branches, coalesce with one another, and in time form a complex tubular network extending in a curved plane from the region of one external jugular vein to that of the opposite side; this network represents the principal or mandibular division of the primary maxillary lymph sinus. The other divisions, the circumoral, temporal, and pericardial, arise from the mandibular division by outgrowth and extension.

Concerning the development of the jugular lymphatic, in 5- to 6-mm. embryos, the first 3 intersegmental veins, which are dorsal vertical tributaries of the pronephric venous sinus (common segment of precardial and postcardinal veins), become joined longitudinally by interanastomoses and consequently take on a plexiform character. This

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intersegmental vein plexus gives rise to the jugular lymphatic, the important change consisting in its gradual separation from the veins (pronephric venous sinus).

The anterior lymph heart, on either side, arises from a circumscribed portion of the venolymphatic plexus at the level and in the axis of the original third intersegmental vein. The plexiform anlage of the lymph heart becomes transformed into the uninterrupted heart chamber by the expansion and fusion of its interjoined channels.

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**The Pattern of the Hair in Unioval Twins.**

*Eugen Ludwig, Anat. Anz., 55:1, Jena, Jan. 2, 1922.*

The difficulty of proving or disproving identity or mirrored likeness in different individuals has led investigators to look for properties which can be measured, weighed or counted, and the slightest variation of which would attract attention. The pattern of the hair with its convergent and divergent whorls offers characteristics of that kind and was therefore employed by Ludwig as a basis for the comparison of a pair of twins. These were 2 male (unioval) fetuses, measuring 28 cm. from vertex to heel, with common chorion and separate amnions. The umbilical vessels of the two fetuses were interlaced. The similarity of the pattern of the hair in these twins was very great. Certain characteristics, which were identical in that respect, whereas they usually are of an entirely different configuration, may be supposed to have had their origin in the close relationship; these included the frontal cross, frontal whorl, median center on the upper lip, perineal tufts, pectoral spirals. Nevertheless, the two twins cannot be described as identical, since there were also many differences between them in regard to the configuration of whorls. Wilder, who examined the system of cutaneous ridges, has arrived at a similar conclusion.

Mirrored likeness could be established between these twins only in one place and only approximately. Their similarity has its origin in the fact that unioval twins are developed from the same germ; the disparities must be accounted for by minimal differences in the distribution of the primordial cells. Absolute uniformity of this distribution is a borderline case, the occurrence of which is very improbable.

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**On Certain Features of Spermatogenesis in Amphibia and Insects.**

*Robert H. Bowen, Am. J. Anat., 30:1, Jan. 15, 1922.*

To determine the true relations of the Golgi apparatus (plus idiosome), acrosome and centrioles, Bowen undertook this work using as his material a single species, *Plethodon cinereus*, Green. It was found that the acrosome of the urodele sperm arises as in many other animals from the Golgi apparatus plus idiosome (acroblast), which is later cast off and remains for some time in the cytoplasm near the base of the sperm nucleus. The middlepiece of the sperm is derived from the so-called proximal centriole.

Bowen's studies on coleoptera were confined to a single species.  
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He found that the acrosome arises in connection with the Golgi apparatus plus idiosome, in a manner similar to that described in several other animals. The nebenkern passes through a series of condensation phenomena similar to those of the hemiptera, and is completely divided only with the disappearance of the chromophilic substance.

To clear up the problem of the acrosome in orthoptera, a few species from the families acrididae and tettigoniidae were examined. In the family acriditae the exact method by which the acrosome is produced has not been made out. Bowen believes that instead of the Golgi bodies fusing to form a single acroblast from which the acrosome is differentiated in toto as in most animals, each Golgi body is an acroblast in itself and the acrosome arises as a fusion product of the portions contributed by each such acroblast.

Under the head of Family Tettigoniidae, Bowen discusses the method of acrosome formation in *Ceuthophilus maculatus* Harris. He has not as yet obtained satisfactory Golgi preparations of the spermatocytes and earliest spermatid stages. During the first steps in the condensation of the chromophilic substance, however, the acroblast in the form of a single compact sphere appears in the cytoplasm in its accustomed location in the angle between nucleus and nebenkern, indicating an origin from the fusion of scattered Golgi elements. The differentiation of the acrosome begins immediately, and a small vesicle soon appears in connection with the acroblast. The position of the acroblast-acrosome complex with reference to the nucleus is not constant as in the hemiptera. Shortly before the nucleus begins to form the sperm head, the acrosome vesicle becomes applied to the anterior surface of the nucleus, the acroblast still maintaining its original attachment to the acrosome. Soon the acrosome flattens out on the surface of the nuclear membrane and its connection with the acroblast is severed. The latter quickly migrates to the base of the head and thence moves backward along the tail exactly as in other insects. The acrosome, already in its definitive position, rounds out to form a knob-like apical piece.

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**The Importance of Dextrose in the Medium of Tissue Cultures.**

*Margaret Reed Lewis, J. Exper. Med., 35:317, March 1, 1922.*

For this investigation over 500 cultures of the connective tissue of chick embryos were prepared in mediums from which dextrose had been omitted or which contained from 0.25 to 5% of this substance. To facilitate the recognition of any abnormal structures that might arise in the cells as the result of other factors in the medium, it was necessary to determine the structure of the normal connective tissue cell. For this, sections of chick embryos and films of fresh embryonic tissue were used. The normal cells did not contain either vacuoles or specific granules. When the abnormal cells were placed in certain mediums, other structures made their appearance, both vacuoles and granules, also giant centrospheres, blebs, liquefaction of the homogeneous cytoplasm, and an accumulation of fat in the cells.

The effect of the lack of dextrose upon the cells of tissue cultures was definite and pronounced and inevitably resulted in the production (Sec. 1—Page 570)

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of vacuoles? The addition of small amounts of dextrose delayed the formation of vacuoles and prolonged the life of the culture. The addition of large amounts (2-5%) prevented vacuolation of the cells, but so much dextrose usually led to a change in the hydrogen ion concentration of the culture resulting in an acid condition which arose coincidentally with the degeneration of the cells.

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**A Three Months Old Strain of Epithelium.**

*Albert Fischer, J. Exper. Med., 35:367, March 1, 1922.*

The purpose of the experiments was to obtain a pure strain of epithelium and to keep it permanently in vitro, as has been done with connective tissue. The strain of epithelium described here was isolated from chick embryo eyes. Fragments of tissues were taken from different parts of the eye, tapetum layer, cornea, and lens, in the hope of obtaining pure epithelium. The lens itself did not grow but the fringe of iris which sticks to the lens when enucleated grew out apparently as pure epithelium. The outgrowth of new cells appears in fine mosaic structure. When cultivated on the free surface of the plasma clot, the new growth appears as a continuous sheet of cells in pavement formation. When cultivated in the middle of the clot, smaller and larger peninsulas of cells grow out and sometimes a few single cells. The reason for the disappearance of epithelium when cultivated in vitro is purely a matter of mechanical conditions. In the periphery of ordinary, well-grown epithelial cultures, made on the surface of the clot, some more or less elongated, spindle-shaped cells appear. These are found mostly when the outlines of the growth reach the outlines of the moist surface. They then embed themselves in the solid clot and become elongated because of the dense medium. The optimum condition under which epithelial cells grow in vitro is on the free surface of the plasma clot under a film of embryonic tissue juice. The epithelial cells have not dedifferentiated. Although the strain is three months old, they grow as a pavement membrane and have kept their epithelial characteristics.

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**Endothelium in Tissue Cultures.**

*Warren H. Lewis, Am. J. Anat., 30:39, Jan. 15, 1922.*

These studies are of the endothelial cells that migrated from the explants of the livers of chick embryos of five to ten days' incubation. The cultures were made in the usual manner with Locke's solution, 80 c.c., plus chicken bouillon, 20 c.c. They were then treated with various chemicals after the incubation period was over, preparatory to being photographed. In general, the endothelial cells migrated from the liver explants to the cover-glass in the form of a loose reticulum of elongated cells that were more or less adherent to one another by their extremities and processes. The character of this reticulum varied considerably in different cultures and in different regions of the same culture. The contrast between the endothelial cells and the liver cells was always quite marked, but it was very difficult to determine whether the reticulum formed by the endothelial cells was a syncytium or not. In young cultures the mitochondria were mostly in the form

of threads of varying lengths and shapes and often with no definite orientation. The conditions of the mitochondria in different cultures of the same age, and even in different cells of the same culture, varied so much that a general description of their appearance is difficult. Granules and vacuoles were found to gradually accumulate in these cells at a rate varying in different cultures. The centriole was not observed in the living cells, but in the fixed material could often be recognized near the nucleus as a small granule about which the mitochondria and neutral red granules tended to accumulate. In older cultures there frequently developed about the centriole a centrosphere which gradually enlarged. The nuclei were oval in form, long and narrow in the elongated cells, and short and plump in the spread-out flattened cells. The contour was usually smooth but in older cultures it was often uneven, being more or less irregular and indented. This appears to be the first indication of the process of budding and amitosis which results in the splitting of the nucleus into several smaller nuclei. The nucleoli varied in number from 1 to 4 and also varied in position, size and form. In some of the older cultures the nucleoli were extruded from the nucleus, usually from one end. In the living cultures both ectoplasm and endoplasm appeared homogeneous; but the endoplasm became very finely granular on coagulation and in it were embedded most of the mitochondria and granules.

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**Classification of the Senses.**

*Hjalmar Oehrwall, Skandinav. Arch. f. Physiol., 42:1, Berlin, Jan., 1922.*

The senses are to be classified according to perceptions, with due regard to the fact that there are simple and complex perceptions. Fundamental perceptions are only those which are not susceptible of reduction, by experimental analysis, into simpler ones. Similar perceptions are grouped, according to Helmholtz, into modalities, senses. The author's point of view, first enunciated some time ago, is defended anew against opposing views of Nagel, Kiesow, Henning and others. There is a fundamental agreement with Asher's exposition.

The opponents' arguments rest on numerous misunderstandings and misconceptions. It was previously thought, for example, that it could be readily, purely intuitively, decided what a sensation is, as distinguished from a complex psychic event. Furthermore, no distinction was made between simple sensations (not reducible to simpler component parts) and sensation complexes or even imaginations. And it was thought possible to decide readily to which sense a given sensation belonged, entirely losing sight of the fact that it is useless to attempt to classify sensation complexes which may partake of the attributes of various senses, and that only after a thorough analysis has disclosed the simple component sensations can there be any thought of classifying these sensations under their respective senses. The error was also made of regarding each sense as a more or less complete analogue of another, an obvious fallacy. For nothing justifies the assumption, for instance, that every other sense is susceptible to differences and shadings of quality, simply because that is true of one particular sense and that within one modality (such as sweetness or touch).

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there must be differences in quality simply because this is true of color perception. It appears quite certain that color vision developed gradually from a much simpler sense, a sense of light, devoid of finer qualities. To this day the human eye contains two such primitive sense organs, the color blind rods and cones in the periphery of the retina; these are certainly rudiments of the simpler sense organ from which color vision gradually developed.

It is equally preposterous to assume that every sense is composed of minor qualities, judging merely by analogy with some sense that is so constituted. It is well known that musical notes form an uninterrupted series, the qualities of which vary uniformly throughout the series. But quite obviously this is not the case with colors, variations of which are quite different and beyond comparison. All attempts to discover within the color range gradations and properties exactly corresponding to the consonance and dissonance of notes, with musical harmonics, etc., have resulted negatively, being founded on no other basis than the a priori assumption of an analogy between the two senses. The same may be said about the assumption that, since phenomena of contrast and compensation have been demonstrated in one sense, these must occur with all senses; or conversely, that whenever these contrast and compensation phenomena do occur in certain sensation qualities, these must belong to the same sense. Such and other similar a priori assumptions are absolutely unjustified. It is not gainsaid that at times it may be desirable to attempt to determine whether a contrast or other phenomenon may or may not be elicited in a given case. But to assume that it must occur is a fallacy. On the contrary, the greatest divergencies in this and other factors may be expected between the different senses.

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**The Ionic Theory of Irritability. The Ionic Theory of the Stimulation of the Organs of Hearing.**

*Lasareff, Pflüger's Arch. f. d. ges. Physiol.*, 193:1, Berlin, Dec. 8, 1921.

The ionic theory of irritability has so far led to the establishment of laws concerning the stimulation of nerves, muscles and of the eye during vision in the dark. The theory assumes that the minimal stimulation depends upon a definite relationship between the stimulating and inhibiting ions; if the former is denoted by the symbols  $c_1$  and the latter by  $c_2$ , while  $c_0$  and K are made to represent the constants, the following formula is obtained (Loeb's law):  $K = c_1 \div (c_2 + c_0)$ .

To test the validity of this law as regards the organs of hearing, a telephone was employed, by means of which appropriate sounds were produced, while the sensation of hearing was determined by means of another apparatus, the intensity of sound being varied at will by means of an attached rheostat. The general theory of the irritability of the organ of hearing assumes that the vibrations of the fibrils of the organ of Corti result, through a chemical process by which ions are set free, in a stimulation of the end organs of the eighth nerve. This assumption leads to the formulation of this equation,  $EU_1 = c_0 \div B - K$ , where E indicates sensation and  $U_1$  the vibratory energy of the fibrils. The values obtained experimentally correspond very satisfactorily to those obtained by calculation based upon the formula given.

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**Electrical Instruments and Phenomena in Physiology.**

*A. V. Hill, J. Roentgen Soc., 17:69, London, Oct., 1921.*

There are 2 sides to be considered: the electrical phenomena themselves, and the electrical instruments used in physiology. (1) The electric current remains the only means at our command of investigating the effects of excitation of the living tissue. Therefore it is important to know how the electric current actually excites the tissue. A constant current excites only when it is made or broken. At the "make," it excites only at the cathode; conversely at the "break." An alternating current excites at each rise and fall. It has been found that there must be a certain quantity of electricity or no excitation will ensue, and also that excitation depends on the rate of change. Thus there are 2 factors. A certain minimum of electricity has to be supplied, and at more than a certain rate. This means that there is an opposition to the current, due probably to diffusion and osmosis of the ions in the cells. Hill states that the Nernst theory of excitation is the one which explains more facts than other theories, and is nearer the truth. The work of Ketih Lucas on the excitable substance of the sartorius muscle of the frog is shown. The curves seem to indicate that, in stimulating the muscle as a whole, one is liable to be stimulating various other substances, nerves, muscles and nerve-endings, which have different duration and strength relation.

What is the nerve impulse? In terms of physics, it is presumably a single wave, traveling at about a quarter of the velocity of sound. Its effect is manifested by the muscle at the other end, but it is accompanied by no physical or chemical phenomena that we can detect except the electrical one. If it produces heat, it is not much more than 100 millionth of 1 degree. It is possible to calculate the energy, however, and from that, the amount of heat set free, and that is about 1/3000 millionth of 1 degree Centigrade.

Progress in instrument design has proceeded towards the replacement of mechanical by electrical and photographic methods. The string galvanometer is an example. Examples of other delicate instruments and curves and tables showing the progress of the science, are given.

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**The Secretion of Sweat. Part I. Supposed Nerve Fibers on the Posterior Nerve Roots. Secretion After Denervation.**

*J. N. Langley, J. Physiol., 56:110, London, Feb. 14, 1922.*

Langely observed that the injection of Ringer's fluid into the pad of a cat's foot usually caused an even greater secretion of sweat than did the injection of adrenalin solution. Such a secretion was obtained whether the nerves were cut or not. Stimulation of the peripheral ends of the posterior roots of the sixth and seventh lumbar nerves caused no secretion. In contrast to the purely local secretion-stimulating effect of adrenalin and Ringer's fluid, pilocarpin when injected has a widespread effect, always slightly decreased by denervation.

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**The Influence of Water Drinking on the Insensible Elimination of Water by the Skin.**

*O. Moog and E. Th. Nauck, Ztschr. f. d. ges. exper. Med., 25:385, Berlin, Dec. 15, 1921.*

On the strength of 5 series of experiments carried out with the large Schwenkenbecher box, by means of which the water elimination of the entire body surface, excepting the head, is determined hygrometrically, the authors report on the influence of water drinking on the elimination of water by the skin. The individuals for the experiment were first restricted to a definite amount of fluid for several days, different individual requirements of fluid being taken into consideration. Thirst, as well as any other discomfort, must be avoided. Immediately before the experiment, 800-1000 c.c. weak tea at 30° C. was given, to determine the influence of a single increased supply of liquid. A box temperature of 25° C. was the one best liked by the individuals. The experiments show that the insensible elimination of water by the skin, at the same temperature and with slight variations of relative humidity, depends on the amount of fluid imbibed. This increase of insensible water elimination by the skin persists for only a short time, until the organism has accommodated itself to the increased water supply. The period of increased insensible cutaneous water elimination varies in different individuals, lasting only two days in some, in other cases three times as long. After a daily water supply of 3000 c.c. has continued for several days, the increase of cutaneous water may amount to 7-40%. A single increased supply of liquid of about 1000 c.c. does not alter the insensible water elimination by the skin, neither after a long drinking period nor after relative water deprivation lasting several days, as in the first case the kidney eliminates excessive water in a few hours and in the second case water retention supply. The period of increased insensible cutaneous water elimination in the tissues takes place. Psychoneurotic disturbances influence cutaneous water elimination to a high degree.

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**The Influence of the Relative Humidity of the Air on the Insensible Elimination of Water by the Skin.**

*O. Moog, Deutsch. Arch. f. klin. Med., 138:181, Leipsic, Jan. 24, 1922.*

Experiments were carried out in Schwenkenbecher's cabinet, the head of the person under observation remaining outside. The excreted quantities of water were determined by 2 hair hygrometers (Koppe) and calculated on the basis of Wolpert's tables. The average temperature was 25° C.; the ingress of air was measured by a gasometer; the quantity of H<sub>2</sub>O contained in the air was raised to just below 100%. All experiments tended to show that the imperceptible cutaneous secretion of water is increased, if the relative humidity is high. Nuttal's apparently opposite results seem to be accessible to interpretation in the same sense. At 25°, the behavior of man corresponds to that of Rubner's animals at 20°. At 25°, in the case of man, the loss of heat by evaporation is already more important than by conduction and radiation; possibly, overheating of the skin takes place at first with further increased evaporation. Under the experimental

conditions described above, therefore, the imperceptible excretion of water does not represent evaporation, but an active function of the body, which regulates its temperature in this way.

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**Voluntary Function of Smooth Muscle.**

*Franz Hamburger, Münch. med. Wochenschr., 69:145, Feb. 3, 1922.*

A number of examples are cited to demonstrate that at least certain groups of smooth muscle are under voluntary control. This is especially shown in the bladder musculature. Every healthy individual can start or stop the urinary flow at will. This shows that the smooth muscle of the bladder may be controlled voluntarily. The same must be true for other sets of smooth muscle, provided that the function of the muscle can be consciously observed, as in the case of the bladder. There are individuals who can relax their gastric muscles and resume the contractions to various degrees. They can swallow air and expel it in suitable quantities. Man can learn to control his gastric musculature because he can observe it with his senses, by hearing the activity as well as by seeing, feeling and tasting it. Goose skin may be produced by imagining coldness or the scratching of a slate pencil. Cross-striated muscles are not always as much under voluntary control. A unilateral contraction or relaxation of the abdominal muscles is not possible. This is an example of incomplete control of striped muscle. We use our muscles, smooth as well as striated, only in relation to the noticeable manifestations.

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**A Convenient Electrode for Experimental Electrocardiographic Work.**

*Carl S. Williamson, Arch. Int. Med., 29:274, Feb. 15, 1922.*

There is no necessity for making an incision in the animal's skin in order properly to insert this electrode. Time is saved, an infected wound avoided, anesthetizing is unnecessary. The electrode is a cuff made of copper plate; width of cuff  $1\frac{3}{4}$  in., minimum diameter 1 in. It is flexible, easily bent to fit around the leg of the animal and is held by a thumbscrew. The connection of the lead wire to the cuff is secured by soldering a copper rivet to the outside of the electrode; the rivet is threaded and provided with lugs to hold the lead wire. The animal's leg is shaved, excess dirt removed and the cuff snugly adjusted. A large series of experiments has shown not more than 1,000 ohms resistance, and the electrode has proved in all respects an improvement over the type generally used.

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**The Regulation of the General Circulation Rate in Man.**

*C. G. Douglas and J. S. Haldane, J. Physiol., 56:69, London, Feb. 14, 1922.*

These experiments represent the completion of work begun and reported by the authors in 1914. In the previous paper the authors gave data, calculated from the carbon dioxide pressure of the oxygenated venous blood in the lungs, showing that for 3 male subjects the car-  
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bon dioxid pressure of the venous blood for oxygenation, after ten minutes' rest on a chair, was about 5 mm. above the arterial carbon dioxid pressure. Calculated on the basis of the dissociation curve, the extra charge of carbon dioxid per 100 c.c. of venous blood was only 3.15-3.3 c.c., or 21-22% of the extra charge which would be present if all the oxygen of the arterial blood had been utilized for the production of carbon dioxid. This gave a calculated circulation rate of about 7.7 liters per minute, which was much higher than the rate given during rest by the nitrous oxid method. In order to check their figures the authors proceeded, in 1914, to determine directly both the true carbon dioxid pressure and the true oxygen pressure of the venous blood. Many of the earlier experiments were, however, unsatisfactory, as only one preliminary breath was employed, and it was not until the authors employed 3 breaths that consistent results were obtained. Various preliminary experiments were also required in order to discover the proper proportions of both oxygen and carbon dioxid in the gas mixture to be employed. It is evident that unless both of these proportions are about right it is impossible to measure directly and accurately either the true oxygen pressure or the true carbon dioxid pressure of the venous blood.

The method which the authors adopted was first to obtain, by a pilot experiment, the approximate composition of the gas mixture required to produce equilibrium with the venous gas pressures. A mixture of this composition is then prepared in a Douglas bag with the help of 2 or more gas-meters, and 2 or 3 experiments are made with it, the depth of the preliminary inhalations being somewhat varied, so that the gas percentages in the alveolar air are slightly higher or lower in the different experiments, and are thus slightly above or below the venous gas pressures. The actual venous gas pressures are thus "straddled" and can then be calculated from the rise or fall of the gas pressures in the second alveolar samples as compared with the first. As an alternative method, particularly when only the carbon dioxid pressure of the oxygenated venous blood is being determined, 3 bags of mixture are prepared, differing by about 0.5% in carbon dioxid content, and an experiment is made with each bag. In making an experiment a deep expiration is first made, followed instantly by a deep inspiration from the bag, another deep expiration into the air and inspiration from the bag, and a final deep expiration into the air and inspiration from the bag. The last inspiration is held for two seconds, and a sample of alveolar air is taken at the end of a sharp expiration of about 1600 c.c. Just after or before the experiment, the subject remaining under exactly the same conditions, the metabolism is determined with all the usual precautions, by means of the Douglas bag method. Samples of alveolar air for the determination of arterial carbon dioxid pressure are taken as nearly as possible at the same time and under the same conditions as the samples for venous gas pressures. The authors used the Haldane-Priestley method of directly determining the carbon dioxid pressure of the alveolar air, inferring from this the carbon dioxid pressure of the arterial blood. Several experiments were performed to test the assumptions on which the method is based.

From the tabulated data the authors calculated the circulation rate. In the experiments on the venous blood before oxygenation the venous blood was found to have gained 62 c.c. of carbon dioxid per liter of

blood; the production of carbon dioxide per minute was 546 c.c. Hence the circulation rate, calculated from the carbon dioxide results, was 546 divided by 62, or 8.8 liters per minute; and as the pulse-rate was 77, the output of blood per heart-beat was 114 c.c. The oxygen data may be calculated as follows: The venous blood had lost 72.9 c.c. of oxygen per liter of blood, and the consumption of oxygen was 621 c.c. per minute. Hence the circulation rate was 621 divided by 72.9, or 8.5 liters per minute, and the output per heart-beat was 110 c.c.

The authors also observed that during work there is a great rise in the percentage utilization of the oxygen in the blood, and that owing to this the general circulation rate does not increase in direct proportion to the general metabolism. A moderate excess of carbon dioxide in the inspired air does not appreciably increase the circulation rate, although it does increase the respiration.

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**The Heat Liberated by the Beating Heart. III. The Oscillations of Temperature during the Cardiac Cycle, or the Thermocardiogram of the Terrapin.**

*Charles D. Snyder, Am. J. Physiol., 59:254, Feb. 1, 1922.*

It has been previously shown by the author that the temperature of the terrapin's surviving ventricle rises and falls with each beat with a regularity and apparent smoothness equal to the mechanical changes of the beat. The question the author wished to decide in this work was, would the temperature graph continue to be so simply diphasic if the heart were made to beat more slowly, thus giving a very sensitive galvanometer more time to follow the detail of temperature oscillation. To secure details of temperature changes during the single cardiac cycle, one must select either a galvanometer of very short period or a heart beating at a slow rate. In this work the latter alternative was used. The set-up of apparatus for the experiments enabled the author to have on drum records the following data: (1) The performance of the isometric lever, zero tension, initial tension; (2) the various tensions developed during the heart's activity over a period of time, or the cardiomyograms; (3) the performance of the galvanometer, the steadiness of the null point over a period of time and the frequency of serious external disturbances, the promptness of response and the distance of deflection to a current of known strength (the sensitivity), the period of time required for this deflection, the amount of dead beat or aperiodicity prevailing; (4) sometimes the prevailing difference of temperature between the cold and warm junctions of the thermopile a half-hour after it has been placed in the heart is so small that the swing of the galvanometer from null, when the thermopile is thrown in the circuit, can also be registered on the drum record; (5) by means of the apparatus Snyder was able to register synchronously with the myocardiogram the accompanying temperature changes of the ventricle during the transitions from systole to diastole, through the pause, and back again to systole, in short, the thermocardiogram.

From a study of the graphic and tabulated results one learns that the following points have been brought out in the investigation: When the muscle temperature of terrapin heart beating at sufficiently slow rates is observed, there appear oscillations of temperature that are  
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characteristic for the various mechanical phases of the cardiac cycle. These oscillations fall into 6 distinct phases. The series for a single heart beat as traced in the graphic record is termed a thermocardiogram. The durations of the phases of the thermocardiogram as well as the temperature changes and heat values they represent have been measured and calculated by the author and finally compared with the successive mechanical events of the cardiac cycle. The heat values of the thermocardiographic phases have further been compared with the heats of reaction as demanded by the chemical events now known to occur during the activity and recovery of frog skeletal muscle in long-continued experiments and as determined and outlined by Meyerhof. From these comparisons it is shown that the rise of temperature during systole (rise of muscle tension) is more than is demanded by the sums of the heats of the anoxidative reactions. The excess of heat has been ascribed to, and has been shown in large part to be accounted for by, the thermo-elastic effect of the isometrically contracting muscle. During diastole a remarkable fall of temperature occurs in the thermocardiogram that can be accounted for only in small part by the reverse thermo-elastic effect just alluded to. After considering the probable fall of temperature due to the nature of the thermopile used and the duration of the phase, and the possible cooling due to experimental error the author concludes that about three-fourths of the temperature fall in this phase must still be due to endothermic processes going on within the muscle whose nature is still undetermined.

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**The Effect upon the Cold-Blooded Heart of Changes in the Ionic Content of the Perfusate. I. Upon the Normal Mechanism. II. Upon the Arrhythmias.**

*E. Cowles Andrus and Edward P. Carter, Am. J. Physiol., 59:227, Feb. 1, 1922.*

The authors performed these experiments in an attempt to analyze the various types of arrhythmias experimentally produced in the cold-blooded heart, more especially their association with changes in the ionic content of the perfusing fluid. The terrapin's heart was used because a specialized conducting mechanism is lacking in the ventricle and changes in conduction of the excitatory process can therefore be taken as due to alterations in the conductivity of the muscle itself. The terrapin were pithed and the plastron removed. A small cannula with a 7.5 cm. "chimney" was inserted in the superior vena cava and an outflow established through the aorta. Perfusion pressure was regulated by means of Mariotte bottles and maintained at a level just sufficient to cause dilatation of the auricles in diastole and to allow adequate contraction in systole. Ringer's solution was freshly prepared before each experiment. The pH of the solution was determined by adding 5 drops of a 0.01% solution of phenolsulphonephthalein to 3 c.c. of the Ringer's solution and comparing with standard tubes. The reaction of the perfusion fluid was adjusted by adding N/10 HC1 and testing with the indicator until the desired pH was reached. By means of threads attached to the surface musculature and connected with light muscle levers, the right auricle and ventricle were made to record upon a smoked drum. The amplitude of mechanical contraction was the only measure-

ment made upon these records. The mechanical and electrical records were synchronized by an electric timer. In taking the electrocardiographic records a standard lead was used throughout; small nonpolarizable electrodes of kaolin paste containing a saturated solution of copper sulphate were placed in such relation to the heart that they gave the desired axial lead corresponding to lead II of the Einthoven nomenclature. The basal electrode was applied either upon the pectoral girdle, 3 cm. to the right of the median line, or upon the surface of the body just above, and to the right of the right auricle. The apical electrode was applied on the peritoneal surface to the left and caudad to the frenulum. Except where otherwise stated, the string was standardized for a deflection of 1 cm. per millivolt. The authors depended throughout these experiments upon the normal stimulus. The following intervals were measured in each record: (1) R-R, representing the rate of stimulus production at the pacemaker; (2) P-R, giving the rate of conduction from auricle to ventricle; (3) QRS, the rate of invasion of the excitatory process in the ventricle; (4) R-T, as representing the duration of ventricular systole. In addition, the amplitude of R, S, and T and the duration of T were measured. In the later experiments, the amplitude of the mechanical contraction of the auricle and ventricle were added to the above data.

After determining, by means of control preparations set up without using an artificial perfusate and later with normal Ringer's solution, that no significant changes in the intervals as measured could be observed, the authors determined the effect of the following variations: Hypertonicity, obtained by adding sufficient quantity of glucose to double the osmotic pressure of normal Ringer's solution. It was found to produce an increase in the rate of stimulus production, in the rate of auriculoventricular conduction, and to shorten the period of invasion in the ventricle and the duration of ventricular systole. A decrease in the concentration of NaCl decreased the rate of stimulus production, retarded conduction at the auriculoventricular node and diminished the duration of ventricular systole. An excess of NaCl in the perfusate impaired the rate of stimulus production and of auriculoventricular conduction, but the spread of the excitatory process and the duration of ventricular systole are both increased by an excess of NaCl. The effect of a change from normal Ringer's solution to a 0.75% NaCl was studied by the authors. The tabulated results show that with NaCl alone all the phases of the electrical activity are retarded.

Diminution in the concentration of KCl caused a decrease in the rate of the pacemaker, a decrease in auriculoventricular conduction and in the rate of spread in the ventricle. Ventricular systole was prolonged. An increase in KC1 concentration caused the following: The rate of stimulus production was decreased, auriculoventricular conduction was impaired, and the duration of the systolic phase in the ventricle diminished. The rate of spread of the wave of excitation in the ventricle remained unaffected. A decrease of calcium chlorid content (or rather an absence of it from the Ringer's solution) diminished the amplitude of both mechanical and electrical records. The heart rate was retarded and the conduction at the auriculoventricular junction impaired. Calcium chlorid in excess of the normal concentration tends to diminish the interval of stimulus production, to facilitate conduction at the auriculoventricular node and markedly to increase the rate at which

the wave passes off the ventricle. The rate of spread over the ventricle, as visualized in the QRS complex, is retarded. Concerning the arrhythmias (abnormal mechanisms) in these later experiments the authors made no attempt to produce abnormal types of rhythm but when such occurred they were recorded and studied. Subsequently the electrical records were measured with a view to studying the changes in the various phases of the course of the wave of excitation coincident with the alteration in rhythm. The authors remark that it soon became apparent that there was nothing typical about the arrhythmia produced by a given change in the perfusate.

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**The Measurement of Intravenous Temperatures.**

*Harry Clark, J. Exper. Med., 35:385, March 1, 1922.*

Clark describes his apparatus devised for the purpose of accurately determining blood temperatures. The temperatures are measured by a thermo-electric method, in which one makes use of the fact that the discontinuity of electric potential at a junction of 2 dissimilar metals depends only on the nature of the metals and the temperature of the junction. The thermo-electro-motive force may be used in either of 2 ways to measure temperature; (1) directly, by means of galvanometer, potentiometer, and standard cell; or (2) to maintain a current in the circuit which will be proportional to the voltage, and which may be measured by the galvanometer deflection. In the present case the temperature range is small, being only about 5° C. above and below normal, which may be taken as 37° C., and the resistance of the circuit is fixed. For these reasons and in the interest of simplicity and quickness of operation, the galvanometer deflection method was adopted. To use this method to best advantage the second thermocouple is kept constantly at 37° C. by means of a special thermostat. The apparatus consists essentially of the unit containing the couple to be placed in the body, which is referred to as the needle unit; the portable thermostat; the cable connecting the needle unit with the thermostat; and the galvanometer with necessary switches.

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**Humoral Transmissibility of Cardiac Nerve Activity.**

*O. Loewi, Pflüger's Arch. f. d. ges. Physiol., 193:201, Berlin, Dec. 24, 1921.*

Vagus or accelerans stimulation in the isolated heart of cold-blooded animals lends the cardiac content vagus or accelerans activity, i.e., this content, when introduced into a second heart, has the effect of stimulation of the corresponding nerves. The question was, whether the active substances come into existence primarily through nerve stimulation or secondarily through the vagal diastole, i.e., sympathetic increase in function. The experiments were carried out in summer on frogs and toads; with the progress of summer, the vagus action is smaller in the case of the former, and the accelerans action in the case of the latter. The activity of the vagus content in frogs was shown to be weaker as compared with the activity in the spring. Mixed activities are often noticed when vagus and accelerans are stimulated simul-

taneously. One often observes in toads, first inhibitions and then movement stimulation, since the inhibitory substance is probably absorbed rather quickly, its action falling during the latent period of the stimulation substance. The content hearts with normal beats, such as that left in the heart for thirty minutes, proved to be ineffective. Even absolute cardiac rest, by means of Stannius' ligature produces no effective content, so that rest alone cannot be depended upon for inhibitory substances. An analogous condition is found as regards the increase of cardiac activity, but this cannot be proved experimentally, as all agents for hastening heart action might also excite the accelerans. It was shown, however, that the above-mentioned fluctuation between inhibition and increased activity took place not only on stimulation, with mixed results, but also in an inhibitory period lasting for twenty minutes. Thereby quantitative differences between the reactions of the toad and of the frog are revealed. The production of the effective substances is, therefore, dependent not upon the mechanical result of stimulation, but upon the excitement produced by stimulation it precedes the mechanical result of stimulation.

Testing for chlorin content, and comparison of the action of the vagus content in chlorin solutions, demonstrated that the chlorin in the vagus substance is not the important factor but perhaps neurin. By testing the accelerans substances (from toads' hearts, especially) it was shown that Ringer's solution of 0.01% NaHCO<sub>3</sub> had, after accelerans stimulation, decreased in alkalescence, while hydrocarbonate of free Ringer's solution exhibited on alkaline reaction. The alkalescence therefore, is not the determining factor. Calcinated heart content is noneffective. Consequently, we are dealing here with an organic substance. Lipoids do not participate in the action. Apparently, it is a specifically sympatheticimetic substance.

The manner in which the nerve leads to the formation of such a substance is not yet clear. The point of attack of the vagus substance is, doubtless, postganglionic, since nicotin does not check the action; if the point of attack were in the nerve ends, the stimulation of the vagus would cause the formation of a substance which would constantly excite the same vagus ending. The result of nerve excitation would then be a direct effect of this. Probably, however, the point of attack lies in specific portions (receptive substances) of the stimulated organ.

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**The Relation of the Curvature of Vessels and of Hollow Viscera to Their Internal Pressure.**

*Cranston Walker, Brit. M. J., London, Feb. 18, 1922, p. 260.*

In considering the pressure within hollow viscera and vessels, it is overlooked that the curvature of the containing wall influences the pressure within it. Although the principles are familiar in many branches of science, the formulas and physical facts they express appear to be unknown to the majority of medical writers. Formulas expressing the relation between the curvature of a stretched membrane and the pressure it exerts are given; the equations in words are: the pressure inside a stretched membrane is proportional to its tension and curvature, and the influence of curvature as such is emphasized. Static deductions are reviewed, and under the dynamics of the subject 2  
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physical examples are briefly discussed: (1) where the tension of the membranes is not altered by stretching or contraction; and (2) the case of extensible membranes which obey Hooke's law, i.e., tension is proportional to stretch. The author has found from experiments that Hooke's law can only be assumed in physiology as a means to a first approximation.

**Summary:** Pressure exerted by any structure comparable to a stretched membrane is dependent on its curvature. Pressure within a cylindrical and spherical membrane is  $t \div r$  and  $2t \div r$  respectively, where  $r$  is the radius of curvature, and  $t$  the tension. With rubber-like materials, as a curved membrane is progressively distended, pressure rises rapidly at first, then more and more slowly as it approaches a limiting value. Such materials are only a rough guide to the behaviour of membranes made of muscle and other animal materials. In any exact consideration of the mechanics of vessels and of hollow viscera, the curvature of the wall must be taken into account. When such allowance is made, physiological effects will be more clearly visible.

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**The Experimental Foundations for the Conception of Reflex Hypertonia.**

*Walter Frey and E. Hageman, Ztschr. f.d. ges. exper. Med., 25:271, Berlin, Dec. 15, 1921.*

In compression of an arteriovenous aneurysm, or of the femoral artery, rise in blood pressure and slowing of the pulse have been observed; these disappear after lumbar anesthesia. This action is due to irritation of the tissue and takes place also when the vein alone is compressed. Research was made to analyze the factors pertaining to tissue dyspnea. The vessels and nerves of both thighs in anesthetized rabbits were exposed; the musculature was ligated; the nerves of the left leg were cut. Narcosis was interrupted, curare given subcutaneously and artificial respiration applied. Cannulas were then tied in the artery and vein and the extremity was irrigated with normosal to remove the blood. Finally, a cannula was inserted in the carotid artery, which had previously been prepared for the blood pressure tracing. Right intra-arterial injection of 1 c.c. silver nitrate solution caused a fall of 6 mm. Hg in the blood pressure, then a sustained elevation of 26 mm., the curve resembling that seen in stimulation of the vagus. The same injection in the nerveless left leg caused no rise in pressure. This reflex hypertonia is explained by the irritation of the nerve-endings in the tissue, analogous to that produced by other irritations causing pain. The negative result in the nerveless leg shows that the vasomotor center can be stimulated from the periphery. Injection of 0.5 c.c. electrar-gol, or of 1 c.c. cold saturated lead acetate solution, does not raise blood pressure.

No rise in blood pressure is produced by injection of carbonic acid in the form of suffocation blood, or normosal solution saturated with carbonic acid, obviously because carbonic acid is neutralized by tissue alkalis in a state of rest as well as in conditions of fatigue. Blood pressure was raised regularly by injection of 1 c.c.  $\text{N}/_{50}$  or  $\text{N}/_{10}$  monopotassium phosphate solution, also by 1 c.c.  $\text{N}/_{10}$  lactic acid, but there was no action on the nerveless leg. Beside the direct dilatation of the

vessels, acids produce a general exacerbation of irritability of the nervous system as an expression of acid poisoning. Apart from the central regulation of the blood flow, a peripheral one must exist, which supplies the organs with blood by means of centripetal impulses. Lactic acid is stronger than carbonic acid; its action on the contractile processes in the musculature shows that its behavior in the tissues is that of an acid. The experimentally determined active amount corresponds to its physiologic concentration in the tissues. Therefore, the assumption of a reflex action on the vasomotor system by the lactic acid formed during muscular work, in the sense of reflex hypertonia, is rendered probable. Further, it is probable that rise in blood pressure observed in fatigue processes is due to excessive formation of lactic acid, although such an accumulation with a good circulation is not easily comprehensible. To elucidate this matter, special experiments were devised. If the presence of acids induces reflex hypertonia, blood pressure should be raised when an animal is asphyxiated whose brain is supplied not with its own blood but arterially with that of another animal. The experimental requirements were the following: 2 adjacent anesthetized animals, Tracheotomy, curare, artificial respiration, preparation of the cervical veins and carotid arteries, ligation of both subclavians before the origin of the vertebral arteries, injection of cg. hirudin, through cannula in a cervical vein, connection of the veins and carotids from one animal to the other by cannulas, insertion of a cannula (for the blood pressure tracing) in the second carotid of the receiving animal whose head is supplied with blood exclusively by the other animal. On shutting off the air supply from the receiving animal, very slight rise in blood pressure and vagus pulsations are observed, both of which are induced by reflex from the periphery. The slight rise of blood pressure, however, shows that suffocation hypertonia must be looked upon as consisting only in small part of a peripheral irritation by venous blood. Reflex hypertonia cannot be assumed, as the spinal centers, which are partly responsible for the vascular tonus, have not been excluded. It has not been proved, therefore, that the accumulation of carbonic acid in the tissues is able to raise blood pressure by reflex, though an active accumulation of such bodies may take place in pathologic cases. While the injection of uric acid and creatin had no influence on blood pressure, ammonium carbonate and uric acid produced a rise which was absent in the nerveless leg. Under physiologic conditions uric acid and ammonium carbonate are of no importance for vascular tonus. These bodies may raise blood pressure in the presence of bad circulation and injured excretory function. The spastic rise of blood pressure in kidney affections, which is unquestionably related to the retention of nitrogenous bodies, may also occur from irritation of peripheral nerves by products of nitrogenous metabolism, causing reflex stimulation of the vasomotor center. These researches furnish new aspects of the conception of arteriosclerotic and nephrogenous hypertension.

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**The Motor Activity of the Venae Cavae.**

*Russell Burton-Opitz, J. A. M. A., 78:705, March 11, 1922.*

In general, it may be stated that the resistance encountered by the arterial blood in its passage through the vascular system depends  
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upon: (a) the size of the arteriocapillary orifice as determined by vaso-motor action; (b) the size of the capillary blood-bed, and (c) the viscosity of the blood. This subject has been amplified in recent months by assuming that the walls of the veins and venules change their positions not solely in accordance with the height of the venous pressure, but also in an active manner in consequence of motor influences. It is obvious that it must be the output of the heart per unit of time rather than the frequency of the heart which determines the functional capacity of this organ and, in turn, influences the venous flow and pressure.

In experiments on cats injections of epinephrin were made into the femoral vein on the corresponding side, or into the inferior vena cava very close to the right auricle, these tests being repeated after both vagus nerves had been divided. The greatest reduction in the cardiac rate coincided with the period of maximal arterial pressure. At this moment a marked diminution in the second volume of the venous flow developed, which persisted during the entire period of high arterial pressure. These changes led to the belief that the rise in venous pressure is not of local origin, but is due to the establishment of a high peripheral resistance. The latter, in turn, diminishes the minute output of the heart. Accordingly, it seems that these changes cannot be indicative of a motor mechanism in the central segments of the venae cavae.

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**The Application of the "All or Nothing" Principle of Nervous Conduction to the Interpretation of Vasomotor Reflexes.**

*E. G. Martin, Am. J. Physiol., 59:400, Feb. 1, 1922.*

From a review of the literature bearing upon the application of the "all-or-nothing" principle of nervous conduction to the question of whether there are specific pressor and depressor fibers in spinal nerve trunks, it appears that such specific fibers cannot be postulated in the present state of knowledge. From consideration of the reflex vasomotor responses to excitation of nerve trunks with various strengths and rates of stimulation, the conclusion is drawn that the significant factor is the total impulse stream generated within the afferent portion of the nerve trunk in a unit of time. Impulse streams of small or moderate total volume induce reflex vasodilatation; impulse streams of large total volume induce reflex vasoconstriction. In view of the finding of Ranson and his coworkers that the afferent intraspinal tracts are different for depressor (excitodilator) and pressor excitations, it is necessary to postulate such differences between the tracts that moderate impulse streams pass successfully along the depressor tract to the vasodilator center, while only impulse streams of large volume are conducted along the pressor tract to the vasoconstrictor center.

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**Vasoconstriction from Warmth Stimulation.**

*E. G. Martin and L. A. Jacoby, Am. J. Physiol., 59:394, Feb. 1, 1922.*

In a number of experiments in which the lower part of the human body was immersed in water at about 42° C., the immersion was fol-

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lowed in about seven seconds by a drop in temperature of the skin of the small of the back averaging slightly less than 0.2° C. Accompanying this drop in temperature were well-marked "gooseflesh" and sensations of chilliness. The author interprets these findings as evidence that a large volume of nervous discharge, due to stimulation of a great many receptors for warmth, elicits typically reflex vasoconstriction.

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**The Filling Conditions of the Blood Capillaries and the Causes Influencing Them. I. Mechanical Causes.**

*Arthur Hintze, Arch. f. klin. Chir., 118:361, Berlin, Nov. 24, 1921.*

The blood circulation in the living represents a closed vessel tract, all parts of which are completely filled with blood, so far as sections of the vessels have not lost their lumen as the result of compression (from without) or obturation (from within), contraction (with positive content pressure) or collapse (with negative content pressure). The varying distribution of the amount of the blood into the individual vessel areas produces a change in the breadth of the vessel lumen. The resistance in the capillary system as a rule is not so great that the pressure in the peripheral veins originating from the heart sinks to zero or even becomes negative. The pressure in the veins is negative only in the region of the thorax, especially during inspiration. With zero pressure, gravitation alone determines the direction of the circulation, aside from the elasticity of the tissues; but this alone is sufficient to fill capillaries, which have been artificially emptied by pressure, as can easily be shown by experiment. Otherwise there are no absolutely empty capillaries, residual blood is always demonstrable, even with a well applied emptying of blood. Interruptions of the blood stream in the capillaries are explainable by their contraction, by interruption of the blood stream in the afferent vessel and possibly by the absence of erythrocytes for a certain distance (granular circulation). Its origin is probably more likely to be the result of acceleration of the venous outflow. Probably the rhythmical sequence of the "granular circulation" is explainable by the lowering of the blood pressure in the veins during inspiration.

Observations of the capillaries under varying conditions as congestion of all grades, lack of blood and heat show that the contraction of the capillaries in man is independent of the nervous system and that it occurs automatically when the filling of the capillaries reaches a certain stage. If a certain content filling is exceeded, which manifestly may vary correspondingly with the actual wall tonus, contraction results, just as dilatation results from obstruction of the importation and a deficient content. It can be assumed that other mechanical factors also can give rise to capillary contraction independently of the nervous system besides the relative overpressure produced by the content, but additional experiments are necessary in this respect. At any rate, the compensatory content filling is to be considered as the adequate stimulation for normal capillary contractions, produced in the living organism by the left heart and also by the inspiratory suction power, not to the point of underpressure (or if to the point of underpressure, the latter

is entirely transient), or lack of pressure in the capillaries. This facile vessel overfilling therefore is the most important peripheral mechanical factor. The capillary contraction independent of the nervous system can be produced not only by mechanical causes, but on the contrary, thermic and biologic chemical influences no doubt have an important influence upon the vessel wall.

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**The Heat of Reaction of Oxygen with Hemoglobin.**

*Edward F. Adolph and Lawrence J. Henderson, J. Biol. Chem., 50:463, Feb., 1922.*

Gas at a standard temperature and pressure was bubbled through the reacting solution contained in an insulated calorimeter immersed in a thermostat. Temperature changes were read upon a Beckmann's thermometer. The gases used were oxygen, hydrogen, carbon dioxid, and carbon monoxid. A known amount of solution (100 c.c.) at about 22° C. was run into the calorimeter. A non-reacting gas was made to flow through it, and thermometer readings were recorded every sixty seconds. The non-reacting gas exhibited the rate of temperature change due to all constant influences, of which the chief was the small difference in temperature between calorimeter and thermostat. This was the fore period, usually lasting five minutes. Then the reacting gas was run in and the reaction carried to completion, which required eight to twelve minutes usually. A final period was obtained by continuing the passage of the reactive gas after all chemical change had occurred. At completion of an experiment, the thermometer readings were plotted against time. A line through the readings of the final period was extrapolated back to the time when the reaction began. The temperature difference between the extrapolated and the initial readings represents approximately that due to chemical action. For inorganic reactions a greater accuracy was gained by taking the cooling curve for the first half of the reaction period from the readings of the fore period, and only the last half from those of the final period. For rises of temperature of more than 0.5° the method of Pfaundler was used to calculate the cooling correction. Before calculating the heat production it was necessary to know the heat capacities. The capacity of the calorimeter was roughly determined by 3 methods: (1) causing solutions of hydrochloric acid and of sodium hydroxid to react in it; (2) introducing water at known temperatures; and (3) calculating the heat capacity of the glass of which it was made. When containing 100 c.c. of solution with the thermometer and inlet tube in place, the heat capacity of the calorimeter was 14 calories per degree Centigrade. The heat capacity of the solutions was calculated. For inorganic solutions the available data were plotted, and the capacity corresponding to the concentrations read off from the curve. For purified hemoglobin solutions a calculation was made on the assumption that the protein has a specific heat of 0.4 calorie per degree Centigrade per gram when dried. For defibrinated blood, concentrated corpuscles, and serum, the values of Hillersohn and of Bordier were used. The authors remark that the thermochemical method is useful in studying: (1) the location of animal heat production; (2) the velocity of reactions; (3) the

amount of oxygenation and reduction of hemoglobin; (4) the neutralizing power of solutions; and (5) the heat of reaction as applied in the use of van't Hoff's isochor and in the measurement of chemical affinity.

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**The Rôle of Cephalin in Blood Coagulation.**

*André Gratia and P. A. Levene, J. Biol. Chem., 50:455, Feb., 1922.*

Gratia and Levene apply the term cytozyme to platelets or tissue extracts or certain lipoids. In their coagulation experiments they compared the cytozymic function of these 3 substances: ordinary lecithin, lecithin which contained a fatty acid of a high degree of unsaturation, and new cephalin, a substance recently prepared which is free from the decomposition product of lecithin and of cephalin which contains 75% undecomposed cephalin and 25% undecomposed lecithin. The coagulation experiments were carried out by following the routine customary in Bordet's school. Oxalated plasma from which most of the platelets have been removed by centrifugation contains only a small amount of cytozyme and consequently clots very slowly when recalcified, but clots quickly if some cytozyme is given back in form either of platelet suspension, tissue juice, or lipoidic tissue extract. This offers a means of testing the cytozymic properties of a given lipoid by measuring the accelerating influence of the lipoid on the coagulation of a plasma almost free from platelets. When an oxalated plasma has been strongly centrifugalized and then recalcified, the few remaining platelets contain just enough cytozyme to react with but a small part of the serozyme. (Serozyme refers to plasma at the moment of coagulation or serum after coagulation.) Thus only a small amount of thrombin is yielded. The plasma clots slowly and a great excess of unutilized serozyme is found in the serum after coagulation. Such a serum is rich in serozyme and is an excellent reagent with which to test the cytozymic properties of a given lipoid. If cytozyme even in very small amounts is added to this serum, an active production of thrombin immediately results and this mixture is able to clot an equal volume of fibrinogen or oxalated plasma in a few minutes. This is the serozymecytozyme reaction of Bordet and Delange. In the experiments of Gratia and Levene they submitted their different lipoids to both tests. In addition to lipoidic emulsions, oxalated plasma free from platelets, serum rich in serozyme and fibrinogen solution were prepared. Instead of the usual solution of fibrinogen, dioxalated plasma was used by Gratia and Levene as a test for thrombin. It was made by diluting 1 part of a 1% oxalated plasma with 4 parts of a 2% solution of sodium oxalate in saline solution. The tabulated results show that egg lecithin exerts only a slight accelerating influence on the coagulation of recalcified oxalated plasma. After five minutes a mixture of serum rich in serozyme together with cytozyme contains a sufficient quantity of thrombin to clot an equal volume of oxalated plasma in two minutes. But a similar mixture of serozyme with lecithin contains only a practically negligible amount of thrombin that yields scarcely a soft clot after twenty-four hours. Egg lecithin was also found to be inactive at higher dilutions or when allowed to react at longer intervals. No appreciable accelerating inhibiting influence of egg lecithin on the action of cytozyme was found. Identical experiments were repeated with liver lecithin with similar

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results. The mixture containing 65% of pure cephalin had a marked accelerating effect on the coagulation of recalcified oxalated plasma. Gratia and Levene found the cytozymic activity of the mixture of cephalin and lecithin to be extraordinary.

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**Blood Coagulation. IV.**

*R. Stuber and A. Funck, Bischem. Ztschr., 126:142, Berlin, Dec. 27, 1921.*

The blood coagulation can hardly be explained except on a colloidal chemical basis, and, therefore, the conditions of the fibrinogenous flaking were first studied with this in mind. The fibrinogen was produced in accordance with Hammersten's method, and dissolved in a 6% salt solution. In addition, dialyzed fibrinogen was dissolved in various quantities of NaOH and HC1, and called alkali fibrinogen and acid fibrinogen, respectively. First, various precipitation experiments were performed in various neutral salts, and various concentrations. According to the experiments we can express the precipitating effect of the neutral salts, when a neutral fibrinogen solution is employed, in the series Cs>K>Na>Li>Rb according to decreasing strength. Since the fibrinogen was used in a neutral salt solution, one may insert the series in the transition series according to Hoeber. From the tables given it is clear that the alcohol precipitability of the fibrinogen will be suspended in an acid or alkali concentration of 0.5 to 0.005 normal. Thus, there exists in these acid and alkali fields a very strong hydration and ionization, respectively, of the acid fibrinogen. An expression of the stronger dissociation of the alkali fibrinogen, from 0.005 to 0.005 normal — NaOH, is an evident increase of the interior friction, measured with the vicostalagmometer of Traube. The maximum friction coincides with the suspension of the precipitability of the alcohol. The movement in the scale of the acid and alkali fibrinogen of 0.005 normal — HC1 and 0.005 normal — NaCH, respectively, is cathodic or anodic. Conversion experiments were made with Michaeli's apparatus. The iso-electric point of the salt-free fibrinogen was ascertained to be approximately pH — 5.

Relative to the precipitation of the acid fibrinogen through various anions, the following series was obtained: SO<sub>4</sub>>citrate>acetate>Cl>NO<sub>3</sub>>Br>J>SCN.

In regard to alkaline earth Pauli's well-known series of precipitability is valid: Ba>Sr>Ca>Mg. The influence of heavy metal salts was shown in the appearance of the well-known irregular series. Thus, it is evident that the fibrinogen strictly follows the laws formulated by Pauli and his followers regarding albumin and globulin.

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**The Mechanism of Digestion in Omnivora.**

*Artur Schunert and Fritz Kiok, Pflüger's Arch. f. d. ges. Physiol., 193:16, Berlin, Dec. 8, 1921.*

The muscular structure of the pig's stomach differs in some respects from that of other animals, half of the mucosa consisting of cardia glands. It was thought that different forms of stratification of (Sec. 1—Page 589)

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the food ingested could be obtained. The animals were well fed, and after slaughtering the stomachs were carefully removed and cut in frozen sections. The feeding had consisted of repeated administrations of articles of diet of similar consistency (either hard or soft), as well as food of different consistencies. Through a corresponding variation in the factors determining the position of the food in the stomach, any desirable form of stratification is obtainable. As a rule the various foods range themselves side by side or superimposed, in the order of ingestion; this stratification persists for sixteen hours after the meal; mixing occurs only when the stomach is almost empty and the contents are practically fluid. The stratification depends upon the consistency of the food, the direction of entrance of the morsels of food ingested and the relative sizes of the morsels. The pig's stomach, in spite of the peculiar muscle structure of its wall, which would allow for the occasional wedging in of a food morsel into the contents already present, exhibits no unusual variation in the mechanism of filling.

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**The Activation of the Glandular Stomach of the Fowl.**

*J. B. Collip, Am. J. Physiol., 59:435, Feb. 1, 1922.*

The purpose of this paper is to describe a simple method of obtaining gastric juice from the ventriculus of the fowl and to report the results of some experiments designed to test the effectiveness of various measures in causing the activation of the glandular stomach or proventriculus. The method consisted of the introduction of a lumbar puncture needle into the lumen of the ventriculus or gizzard via a puncture in the mid-line just below the xiphoid process of the sternum. When the needle was in place the trocar was withdrawn and a syringe attached. The contents of the gizzard could then be aspirated and the effect of the injection of organ extracts or drugs could be followed as desired. The degree of activity of the proventricular glands was determined by noting the rate of secretion and the acidity of the juice in terms of the amount of tenth normal sodium hydroxid required to just neutralize 100 c.c. of the juice to Topfer's reagent. The titration was carried out with fiftieth normal alkali. The contents of the gizzard, which were aspirated off immediately after the introduction of the needle, were usually alkaline to Topfer's reagent, but the glands of the proventriculus could be activated to secrete a strongly acid juice by the intramuscular injection of tissue extracts such as those prepared from the proventriculus and duodenum of the fowl, the mammalian gastric mucosa and thyroid gland. The very definite effect of sham feeding and of forced swallowing movements indicate that the chief factor in the reflex stimulation of the proventriculus is the mechanical stimulation of the pharyngeal mucous membrane.

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**Differences in the Digestion by Pepsin of the Frog and of Warm-Blooded Animals.**

*Helmut Müller, Pflüger's Arch. f. d. ges. Physiol., 193:214, Berlin, Dec. 24, 1921.*

There are conflicting data regarding the optimal temperature of peptic action in cold-blooded animals. In order to make this matter (Sec. 1—Page 590)

clear, the action of pepsin on carmin-fibrin was tested according to Grützner's method: a glycerin extract, diluted with water, was prepared from the mucous membrane of the stomach and esophagus of a freshly killed frog; 0.2% HCl was added. The experiments were directed toward the influence of the amount of pepsin and that of the temperature. At 0°C. a higher concentration was found to be advantageous; under higher temperatures, also, the activity increased with the amount of pepsin; however, only up to a certain temperature, approximately 12°C., the difference was no longer of consequence. The pepsin activity first increases with the temperature. With higher temperatures (40°-50°C.) the results are contradictory. It may be stated, however, that the speed of digestion increases with the temperature first quickly, then slowly, so that between 30°-40°C. the difference is very slight. From 60°C. there begins a decrease and, on continued exposure, there is cessation of the ferment action. The optimum for digestion is at 40°C., while temperatures over 75°C. cause the immediate destruction of the ferments. The results agree to a great extent with those obtained for the pepsin of warm-blooded animals. It is, therefore, probable that in both species of animals the same proteolytic ferment is present, although, without chemical characterization, which is as yet impossible, this fact cannot be definitely determined.

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**The Hydrolysis of Sucrose in the Human Stomach.**

*Robert M. Hill and Howard B. Lewis, Am. J. Physiol., 59:413, Feb. 1, 1922.*

The inversion of sucrose in the human stomach was studied by the fractional method of analysis of gastric contents. The subjects were healthy men and women students to whom were administered (after a preliminary protein meal) 5 gm. sucrose in 200 c.c. water through a Rehfuss tube. Samples of gastric content were removed at twenty minute intervals for analysis. The experiments failed to demonstrate the presence in the gastric juice of any agent active in the inversion of sucrose other than the hydrochloric acid. The inversion under normal conditions in man is too slight to be of significance, since carbohydrates leave the stomach too rapidly to permit of prolonged action of the acid. The authors were unable to demonstrate the presence of an active sucrase in gastric contents in spite of the fact that intestinal regurgitation had occurred in many cases as evidenced by the presence of bile.

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**Periodicity of Ferments. The Lipase of the Stomach.**

*E. Sluiter, Nederl. Tijdschr. v. Geneesk., 66:572, Haarlem, Feb. 11, 1922.*

Arrhenius thought that the activity of a ferment preserved outside of the body generally decreased. But investigations made at the laboratory for chemical physiology at Amsterdam show that this is not the case, but that the spontaneous dissolution reveals oscillations which are styled "periodicity." The higher the temperature, the slighter the oscillations. The author has made special experiments in order to ascertain whether all ferments possess the quality of increasing and  
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decreasing in activity. Graphic tables show the results of these experiments. The ferment solution was obtained by grinding the mucous membrane of a calf's and a pig's stomach, and steeping them in water. These preparations were preserved in the ice box. Tubes containing 5 c.c. milk and 5 c.c. ferment solution were kept for twenty-four hours at a temperature of 39°C. in the shaking thermostat. Thereafter, the sebacic acid was measured by means of 0.1 N-lye. The degree of acidity of 5 c.c. milk which had also been turned for twenty-four hours in the shaking mixture was deducted from the result obtained with the mixture. The viscosity of the calf preparation was somewhat greater than that of the pig preparation, the ratio to that of water being, respectively, 5:3 and 3:2. The graphic tables show the oscillations plainly. Sluiter thinks that the periodicity must be taken into account in judging the diagnostic value of various quantities. It will probably be necessary to make a distinction between the digestive ferments and those which have remained for a long time in the body, e. g., those of the blood.

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**The Thermostable Active Agent of Pig's Pancreas.**

*Walter Jones, J. Biol. Chem., 50:323, Feb., 1922.*

The existence in the pancreas of an easily detected thermostable agent which decomposes yeast nucleic acid only as far as its nucleotids, is more interesting in its physiological significance than for any light it throws upon the chemical constitution of nucleic acid. The first alteration that yeast nucleic acid undergoes in its decomposition by tissue extracts is assumed to be the production of nucleotid. How is it, then, that extract of pig's spleen and of other tissues which do not contain the thermostable agent in question, can, nevertheless, bring about the progressive decomposition of nucleic acid with the formation of free phosphoric acid and free purin bases? It would appear either that there are 2 ferments which can decompose nucleic acid into its nucleotids, 1 of which is destroyed by heat, or that the decomposition of nucleic acid by tissue extracts does not proceed along conventional lines.

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**Studies on Secretin. I and II.**

*C. van Eweyk and M. Tennenbaum, Biochem. Ztschr., 125:238, 246, Berlin, Dec. 18, 1921.*

The chemical composition of a series of pharmacologically active alkaloids, such as strychnin and brucin, has not been entirely elucidated. The chemical reactions of others are not known and can only be deducted from their biologic reactions. To these belong the hypothetical products of ductless glands, which are named secretins and are divided into two groups. The first group includes such as are produced by the respective organs for their own use, while the second contains those that are conveyed to the organism with the food. The second group is further divided into two subgroups, one containing preformed secretins in food (as whey and spinach secretins), the other, such as are formed in food during its preparation. Researches by Bickel and Eweyk demonstrate that certain materials (casein, yolk of egg) which yielded no extracts containing secretin show the presence of secretin.  
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after being heated to 150°C. and 170°C. In an experiment on a Pawlow dog similar intense secretion took place after the supply of egg albumin hydrolysate was heated to 300°C. The heating of amino-acids seems, therefore, to lead to the formation of physiologically active bodies, and for this reason they appear to be the mother-substance of secretins. This is shown by the fact that when a series of amino-acids (glycocol, alanin and glutamic acid), possessing no secretin action, were heated to 300°, their injection even in larger amounts showed no secretin action. As the aliphatic amino-acids behaved negatively the investigation was extended to cyclic amino-acids. Tyrosin proved inactive, but when histidin was heated to 300° and the products thus formed dissolved, these became active after injection of a Pawlow dog. In the first half-hour 2.1 c.c., in the second 1.3 c.c. and in the third 0.6 c.c. gastric juice were obtained from 47 milligrams of these. They gave Pauly's reaction with diazobenzolsulphonic acid and had a melting point of 235°. As intravenous injection in rabbits produced an effect on the blood pressure which could not be distinguished from that of histamin, it is probable that the latter was in question.

Experiments were accordingly undertaken to determine whether naturally occurring secretins are identical with histidin. Being easily obtainable, spinach was the first material examined. The biologic effects of extracts of spinach containing secretin were compared with those of histamin solution. Histamin possesses 3 easily observable biologic reactions: (1) the action on the gastric mucous membranes in the sense of a secretin; (2) typical lowering of blood pressure after intravenous injection in rabbits; and (3) contraction of the guinea-pig uterus. The spinach hydrolysate was prepared as follows: 500 c.c. sulphuric acid 20% was poured over 600 gm. fresh spinach. The mass was boiled four hours in the water-bath and allowed to stand until the following day, when it was filtered, neutralized with barium hydroxid, cooled and separated from barium sulphate by filtration. Water was then added in such quantity that 5 c.c. of the liquid corresponded to 30 gm. fresh spinach. Subcutaneous injection of 5 c.c. of this preparation in a fasting dog with gastric fistula gave at half-hourly intervals, 16.5, 38.5, 57.5, 40 and 10 c.c. gastric juice. With a further purified spinach hydrolysate the half-hourly amounts of gastric juice were 7.5, 26.0, 78.0, 78.8, 3.11 and 3.00 c.c. From this it appears that gastric secretion was stimulated by spinach extracts; but there was no lowering of blood pressure after intravenous injection in rabbits, and no contraction of the guinea-pig's uterus. The lowering of blood pressure observed by Bickel is obviously due to the action of incompletely decomposed albuminous bodies. In order to eliminate this, only such hydrolysates were employed as gave a negative biuret reaction. Taking all the results into consideration, it is evident that the characteristic properties of histamin could not be obtained; and the nonidentity of spinach secretin and histamin is thereby demonstrated.

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**Observations on the Motility of the Duodenum and the Relation of Duodenal Activity to That of the Pars Pylorica.**

*Homer Wheelon and J. Earl Thomas, Am. J. Physiol., 59:72, Feb. 1, 1922.*

Experiments were made on 23 dogs on the relation of duodenal  
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motility to the motor activities of the stomach. Graphic records were obtained from both anesthetized and conscious animals following the operation for the placement of apparatus. The operation consisted in placing the chambers of a compound enterograph in the first portion of the duodenum and in the antrum or pyloric canal through an opening in the fundic portion of the stomach. Direct observations on the exposed duodenum reveals the fact that motility, in the duodenum exposed in a warm saline solution, arises as a constriction band on the hepatic surface approximately 2 cm. distal to the pyloric ring, or in the terminal portion of the so-called "duodenal cap" in man. This primary contraction is immediately followed by the contraction of increasing numbers of fibers until finally a considerable portion of the duodenum is in a state of high contraction. This phase is followed by rapid relaxation, which, beginning at the point of primary contraction, passes down over the previously constricted area. The rhythmic segmental activity of the small intestine, described by Cannon, is also readily discernible in the duodenum. The most constant type of motility in the first part of the duodenum, as indicated by the graphic method, was found to be rhythmic segmentation characterized by a contraction and a relaxation phase. The graphic results also show that the factors exciting waves of peristalsis in the stomach are more or less directly responsible for peristalsis in the duodenum, the phases of which bear a definite relation to those of the stomach. Since the graphic records show a progressive series of events in the antrum, sphincter and duodenum which bear a constant and definite time relation to each other, the authors believe that the activities of these three parts conform to the principle of the "law of the intestine." Interpretation of the results lends considerable weight to the "gradient theory of the gastro-intestinal tube" as evolved by Alvarez, inasmuch as they show a progressive series of events in the musculature of the stomach and the first part of the duodenum.

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The Myogenic Nature of the Rhythmic Contractions of the Intestine.

Walter C. Alvarez and Lucille J. Mahoney, *Am. J. Physiol.*, 59:421, Feb. 1, 1922.

Review of the literature on rhythmic tissue reveals that most writers quote Magnus' early work to the effect that the rhythmic contractions of the intestine are neurogenic in origin, overlooking the fact that in later experiments he was able to get good contractions from well denervated muscle. The authors studied the rhythmicity of circular muscle of the dog's intestine, stripped away from the longitudinal intestinal muscle twenty-four hours after the bowel had been placed in the ice-box. They were able to get rhythmic contractions from such muscle which they were certain had been freed from all traces of the nerve net. In work with delicate galvanometers they demonstrated that strong rhythmic action currents were being developed in segments of intestine which, so far as the eye could see, were absolutely quiet. These currents are so nearly equal in intensity to those observed in active segments that it can scarcely be argued that they arise in the nervous tissue, the mass of which is small.

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**The Activities of the Intestinal Musosal Motor Mechanism.**

*C. E. King and Lloyd Arnold, Am. J. Physiol., 59:97, Feb. 1, 1922.*

This work was undertaken for the purpose of inquiring more fully into the types and varieties of movement manifested by the mucosa of the dog's small intestine, and to investigate the nature and the control of the mechanism involved. Since it is practically impossible to record movements of the intestinal mucosa, the authors adopted the method of observing the field through an extension binocular microscope, using a magnification of 25 diameters, the field of observation being lighted by a small arc light. The results were recorded as dictated by the observer. The effect on the irritability and activity of the intestinal mucosa of the dog, under the following types of stimuli was studied: mechanical and thermal stimulation, local application of irritants and drugs, influence of extrinsic nerves, intravenous injection of certain drugs. The authors found that the intestinal mucosal motor mechanism is set into activity by mechanical stimulation, by heat, irritants, and by epinephrin, pilocarpin, atropin, nicotin and barium. The mucosa as a whole exhibits movements which may be designated as ridging, grooving and pitting. The movements of the individual intestinal villi (rhythmic shortening, lengthening and lateral movements) may or may not be associated with movement of the mucosa as a whole. Impulses by way of the vagi do not reach the mucosal musculature. The splanchnics carry tonus impulses to the mucosa. The authors believe there is no definite interdependence or correlation between the activities of the outer and mucosal motor mechanisms. They found the mucosal motor mechanism to be most active and reactive in the duodenum and upper jejunum, less so in the lower jejunum and almost refractory in the ileum.

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**Effects of the Galvanic Current on Segments of Intestine.**

*Walter C. Alvarez and Lucille J. Mahoney, Am. J. Physiol., 59:431, Feb. 1, 1922.*

It occurred to the authors that inasmuch as the intestinal segments show a polarity, similar to that found by zoologists in small water organisms, they might show a somewhat similar behavior when placed in the path of an electric current. Accordingly in a series of experiments, segments of rabbit's intestine about 10 cm. long were put into a flat dish full of warm Locke's solution and the current from 2 dry cells was led in through copper wires. When placed transversely across the path of the galvanic current the sections of the rabbit's bowel showed a galvanotropism due to a greater stimulation of the longitudinal muscles on the cathodal side. When a segment was placed longitudinally in the path of the current peristaltic waves began at the cathodal end and ran to the anodal. The direction of peristalsis could be reversed by reversing the current. The authors believe these experiments lend support to the gradient idea of peristalsis because they show that the direction of the intestinal waves can be reversed by an electric current which reverses the gradient of muscular activity.

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**Studies of Liver Function. III. Phenol Conjugation as Influenced by Liver Injury and Insufficiency.**

*K. F. Pelkan and G. H. Whipple, J. Biol. Chem., 50:513, Feb., 1922.*

The general plan of Pelkan and Whipple's experiments was as follows: a dog was first standardized, either after several days of fasting or several days of carbohydrate diet, in order to determine the time required by the liver to conjugate the standard dose of p-cresol. Liver injury was then produced by one of a number of methods and another test was made to observe the capacity of the injured liver. Any satisfactory liver function test must include some factor of strain or load to determine the upper limits as well as the lower levels of liver function.

The tabulated results show that the conjugation of phenols in the body is not disturbed by a bleeding period, by the presence of a bile fistula nor by a lethal intoxication (distemper). The presence of an Eck fistula reduces the amount and speed of phenol conjugation. When the liver circulation is further impaired by partial ligation of the hepatic artery in an Eck fistula dog, one may observe a fall in phenol conjugation to 3 or 5% normal. Liver exclusion, therefore, will eliminate phenol conjugation. The presence of a slight liver injury due to chloroform or phosphorus may not modify the phenol conjugation; extensive liver injury due to these poisons always lessens phenol conjugation; and extreme and fatal liver injury (chloroform) will reduce phenol conjugation to zero. Pelkan and Whipple conclude that phenol conjugation is a function of liver parenchyma cells and of no other body cells.

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**Importance and Significance of Hepatic Glycogenesis.**

*H. Roger, Presse méd., 30:145, Paris, Feb. 18, 1922.*

Roger's previous researches have shown that the antitoxic action of the liver depends on the presence of glycogen or glucose in this organ and disappears in particular in animals deprived of food for a long time. Toxic substances which possess or may acquire in the organism a phenolic or alcoholic radical unite with glucose to form glucosids. These are in turn oxidized and are easily eliminated by the kidneys as conjugate glycuronic acids which possess a low degree of toxicity. Roger has also shown that the liver has a destructive action on the bacteria brought to it by the portal circulation. This action likewise disappears when animals are deprived of food for some time. The presence of glycogen in the liver is moreover essential for the transformation of ketonic bodies and of oxybutyric acid and for the destruction of fats and amino-acids. It appears also that albumins may be synthetized in the liver from glycogen and ammonia and that conversely the destruction of albumins may result in the production of glycogen in the liver. Creatin represents a by-product of nitrogen catabolism. It is produced in increasing quantities in fevers, diabetes, intoxications, and is excreted by the kidneys in the form of creatinin. It can be shown that the transformation of creatin into creatinin takes place in the liver and is dependent on the presence of glycogen. Finally, although it is not settled at the present time whether bile is a secretion or an excretion of

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the liver, it is known that hepatic pulp acting on blood pigment produces a special hepatic pigment, but only in the presence of glycogen. Glycogen does not therefore merely represent a store of energy but is indispensable in intoxications, infections and in the affections which may produce acetonemia or acidosis. The good effects obtained from injections of glucose are to be attributed in part to its action on the liver. Surgeons have also shown that untoward symptoms produced by anesthesia which are referable to the liver, may be prevented by the ingestion of carbohydrates or sugar.

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**Do Species Lacking a Gall-Bladder Possess Its Functional Equivalent?**

*Philip D. McMaster, J. Exper. Med., 35:127, Feb., 1922.*

The question has arisen whether, in species of animals lacking a gall-bladder, the concentrating function of this organ is found in the ducts. Observations were made on the mouse and rat, since these animals, though so nearly related, differ in that the mouse has a gall-bladder, and the rat has none. Methods were worked out for the quantitative determination of the pigment against standard solutions, so that pigment could be used as the index to changes in concentration. In the mouse, bladder bile was found to be more concentrated than that from the common duct; in the rat, bile collected during stasis never became more concentrated in pigment than the normal. The gall-bladder, as a reservoir, is lacking in rats; but it was also observed that rat bile contains 8 times as much pigment as does mouse bile from the liver.

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**The Spleen and Digestion.**

*W. Mollow, Hoppe-Seyler's Ztschr. f. physiol. Chem., 17:218, Berlin, Dec. 27, 1921.*

It has always been maintained in the literature on this subject that the spleen swells during digestion and influences gastric and pancreatic digestion, secretion of bile and peristalsis. Mollow reexamines these statements by means of exact experiments. In reference to the influence on gastric digestion: Two dogs contracted gastric fistula and duodenal fistula. The gastric secretion was examined by perfusing bouillon into the dogs after abstention from food for twenty-four hours previous to the perfusion. After fifteen minutes the remainder of the bouillon was removed and the gastric juice allowed to drop out. In the gastric juice that ran out in ten minutes pepsin (carmin-fibrin method) and free and combined hydrochloric acid were estimated. Some days later splenectomy was performed and after the wound had healed the before-mentioned procedure was repeated. No influence of splenectomy on gastric secretion could be determined. In reference to the swelling during digestion and the influence on gastric and pancreatic digestion: Animals having duodenal fistulas and deprived of food for twenty-four hours, had 2 gm. Pepton Witte in 30 gm. water perfused into the small intestine in order to promote secretion of bile, and 50 c.c. tenth-normal hydrochloric acid to stimulate pancreatic secretion. To control peristalsis the animal was fed on meat and the time required for the passing of the last meat remnants out of the stomach was observed.

Then followed splenectomy and repetition of the procedure. Neither biliary nor pancreatic secretions, nor gastric nor duodenal peristalsis were affected by splenectomy. Consequently, the statements in the literature on the subject, relating to the influence of the spleen on digestion, were not confirmed.

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**Vitamins.**

*Ubaldo Sammartino, Biochem. Ztschr., 125:25, Berlin, Dec. 8, 1921.*

The observation that both the rapidity of reproduction and the rapidity of fermentation of the yeast cells are affected in a positive way by vitamins was examined to determine whether the vitamin stimulates the cell or possibly the cell membrane or whether the zymase itself possibly acts in a stimulating way upon the ferment. The question, whether it is the cell or the cell ferment which is stimulated was investigated on the cell-free fermentation in regard to its behavior toward the vitamins, and it was shown that on the addition of vitamin the zymase fermentation was doubled in rapidity and even increased 5 and 8 fold. As zymase consists of the true zymase and the coferment; as the zymase without coferment is in itself ineffective and unable to split sugar; and as coferment by itself is a promoter and hastener; the question arises whether the vitamin acts upon the true zymase or whether the ferment itself acts upon the coferment; and also whether the vitamin action is purely upon the zymase or whether it acts in a similar or perhaps also a sparing manner upon enzymes of other nature.

It was first investigated how the other ferments behave in their activities in the presence of vitamins. Proteolytic and amylolytic ferments and catalase were examined. In the albuminous digestion with pepsin no effect upon the pepsin digestion was noted from the presence of vitamin; probably for the reason that vitamin is destroyed in the presence of a mineral acid or that the high pH inhibits the vitamin in its action upon the ferment. If the effect of vitamin upon the tryptic digestion is examined in the usual alkaline soda solution, it is seen that the vitamin hastens the trypsin ferment in the alkaline medium. Vitamin showed only a slight effect upon the influence of the amylolytic ferment. The experiments with catalase showed that the effect varied markedly according to the reaction of the medium and in the presence of various substances which act in a promoting or inhibitory way. It was therefore shown that the vitamin, just as it promotes yeast fermentation, also promotes the cell-free zymase fermentation, but that the effect on other splitting ferments, is by no means marked if it occurs at all.

According to the experiments of Harden and Joung zymase can be separated into 3 parts: if the zymase is dialyzed or filtered through a colloid filter, a substance is left on the filter which is unable by itself to split sugar in alcohol and carbonic acid; dialysate is also unable to split alcohol and carbonic acid; but if both are reunited the splitting of the sugar can be seen in carbonic acid and alcohol; if, however, the substance found on the filter is previously cooked and then combined with the uncooked filtrate, no fermentation occurs, but if the substance found on the filter is not cooked but combined with the cooked filtrate, fermentation occurs. From this the conclusion can be drawn that in the zymase

also a separation into the true ferment and coferment is possible and that the true ferment is active only in the medium of a substance of the coferment that will stand boiling.

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**The Accessory Nutritive Factors. II. The Significance of the Water-Soluble Extractive Content.**

*Richard Gralka and Hans Aron, Biochem. Ztschr., 126:147, Berlin, Dec. 27, 1921.*

A foundation food composed of flour, casein paper and salts was insufficient in the long run for growing rats by the addition of fat-soluble accessory factors, rich foods, such as butter or cod-liver oil, the growth of the animals was assured. Tests were then made to ascertain what results could be obtained by adding to the same base water-soluble extractives.

It was found that even by small additions of extractives, success may be reached. However, from that process no conclusion can be reached regarding the extent of the need for extractives during a comparatively long period; rather was it shown that continued growth can be attained only through a rich supply of extractives. Since the daily diet of man and beast is never entirely free from accessory nutritive factors, the basic food was constructed on the natural medium of nutrition (flour). A food poor in extractives was used, (HO) composed of 1000 gm. flour, 125 gm. plasmon, salt mixture and 50 gm. paper: in contrast to this was placed a food form (HE) which through addition of 100 gm. carrot-beet extract obtained by autolysis, that is, 5 gm. bran and 50 gm. carrot-beet extract, was very rich in water soluble extractives. It was not to be determined whether through the presence of the second food form, very rich in water-soluble vegetable extractives, growth would be influenced favorably. The experiments were carried over quite a period of time and were performed on 12 animals. Those which were fed with the form HO died quickly, at the latest on the thirtieth day. The animals fed with the additions of extractives were still strong and in complete health after two hundred days. It is therefore evident that the relative content of water soluble extractives is of the utmost importance for measuring the nutritive value of a food. Enrichment with water soluble extractives guarantees a much better development and extends considerably the period of life. Important also is the discovery that a lack of accessory fat-soluble nutritive factors is borne much better when water-soluble extractives are ingested. The younger the animal experimented on, the more significant are the differences. Therefore, when food is poor in such nutritive factors, it is considerably improved by water-soluble accessory food-stuffs. The sensitiveness to the lack of one accessory nutritive factor is increased if another is in insufficient proportion.

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**Accessory Bodies in Cod-Liver Oil.**

*Heinrich Lax, Biochem. Ztschr., 125:266, Berlin, Dec. 18, 1921.*

Albumin, fat, carbohydrates, salt and water do not suffice for the needs of the human organism, which requires additional supplementary (Sec. 1—Page 599)

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bodies of unknown chemical constitution, accessory nutrient substances, known as vitamins. Up to the present time 3 such supplementary bodies are known: (1) an antineuritic principle identical with the water-soluble vitamin B, (2) an antirachitic principle, the fat-soluble vitamin A, and (3) an antiscorbutic principle. Cod-liver oil, long known for its therapeutic value, was examined for supplementary bodies. The researches were carried out with pigeons in which experimental beriberi was produced by nutrition confined to polished rice. The cod-liver oil employed in the experiments was an excellent preparation that had given striking results in rachitic children. From this an alcoholic extract was prepared by agitation for forty-eight hours, which was afterwards concentrated in vacuum, about 11 gm. being obtained from 2 liters of cod-liver oil. Beriberi pigeons were fed on this syrup. All the experiments prove that experimental beriberi can not be cured either by cod-liver oil or by its alcoholic extract and hence that cod-liver oil does not contain an antineuritic principle (water-soluble growth principle B). The supplementary bodies A and B are thermolabile. The inactivation temperature of A varies from 80°-90° C.; that of B is about 120° C. Cod-liver oil is prepared under high pressure in a boiler at 130°C. for several hours. As the A substance is destroyed at 80°-90°C., cod-liver oil, by reason of the method of its preparation, can not possibly contain any A substance. However, not all the therapeutically active antirachitic principle is destroyed at 120°, from which it may be concluded that there is another principle as yet unknown that is not identical with the fat-soluble vitamin A.

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**The Rôle of the Vitamins in Cell Chemism.**

*R. Hess, Hoppe-Seyler's Ztschr. f. physiol. Chem., 17:284, Berlin, Dec. 27, 1921.*

In order to prove that vitamin-deficient nutrition disturbs the normal activity of ferments, Hess determined quantitatively the oxidation in the tissues of normal pigeons and in those fed on polished rice. Living cut tissue reduces m-dinitrobenzol to m-nitrophenylhydroxylamin, which manifests itself by a yellow coloration. The degree of coloration corresponds to the intensity of the respiratory process (i. e., to the transfer of oxygen) and may be fixed on the photographic plate. It is important that the medium (Ringer solution) in which the tissues are placed have a definite reaction. The Ringer solution was sterilized with sodium bicarbonate (0.1 gm. to 100 c.c. Ringer). Pigeons were quickly killed by a blow on the head, decapitated, bled and irrigated with cold Ringer solution from the left or right ventricle; 1 gm. was then taken from each organ, cut with scissors and placed in 10 c.c. cold Ringer solution. The liquid was decanted. The tissue pulp was transferred to a centrifuge tube of 11 c.c. capacity containing 10 c.c. Ringer solution. Each tube then received 0.1 gm. m-dinitrobenzol and a glass bead. The tubes were corked, placed in a water bath for one hour and 4 drops dilute acetic acid added to clear the liquid. The yellow supernatent liquid was centrifuged. A few cubic centimeters were removed with a pipet, transferred to a graduated beaker and photographed. With the aid of an empirical table the observed extinction values were converted into cell values by means of which the formation of m-nitro-

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phenyl may be measured. Results: Kidney, liver and brain tissue respire much more intensively than muscle, heart muscle being the most active of the latter. The tissues of vitamin-deficient pigeons showed respiration reduced about one-half that of normal animals. Pigeons who received vitamins (yeast), after vitamin deficient feeding, still showed diminished respiration in their tissues, except the brain. Although in the different animals and organs the deviation from the average value is very considerable (depending possibly on the animals' age, the duration of vitamin-deficiency symptoms, or the chronic course of avitaminosis), the fact remains that vitamin tissue in the kidney, liver, brain and musculature shows a reduction in respiration. This observation led the author to the belief that, as a similar disturbance is produced by hydrocyanic acid poisoning, which inhibits the activity of ferment, small doses of hydrocyanic acid should produce symptoms of avitaminosis. Actually, sublethal doses of potassium cyanid produce beriberi symptoms in pigeons. Pigeons suffering from avitaminosis are more sensitive to potassium cyanid than normal pigeons. Here one is not dealing with a general reduction of resistance on the part of pigeons fed on polished rice, but the entire scale of progressive beriberi symptoms may be produced by the smallest doses of potassium cyanid. In both cases one deals with an impoverishment of the body as regards respiratory ferment. The symptoms of sublethal potassium cyanid poisoning and of beriberi are so similar that the differentiation of the animals seems impossible. On the strength of these experiments and of the literature, the author asserts that the material principle of the antineuritic vitamin factor must be the mother substance of the cell ferment, and especially of the respiratory ferment. In the case of antineuritic vitamin, traces of iron offered to the organism seem to be involved and utilized for the formation of oxidizing ferment.

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**The Effect of Vitamin Deficiency on Various Species of Animals. II. Observations on the Comparative Vitamin A Requirement of Rabbits, Rats, Swine and Chickens.**

*Victor E. Nelson, Alvin R. Lamb and V. G. Heller, Am. J. Physiol., 59:335, Feb. 1, 1922.*

The first paper of this series reported the production of xerophthalmia in the rabbit and suggested that the requirement of the rabbit for fat-soluble vitamin (vitamin A) is greater than that of the rat. In this paper the authors present data demonstrating this assumption to be a fact. A ration similar to that which was employed in the authors' previous work was used to compare rabbits and rats. The ration was assumed to be complete except for vitamin A. The growth curves presented in the article show that the ration contained enough of this vitamin to support, for a time, slow growth and maintenance without successful reproduction of the rat, however. Xerophthalmia developed in every case after about four weeks on the ration. Another ration lacking in vitamin A content but complete in all other respects did not produce normal growth in rabbits, but did produce a chronic form of xerophthalmia suggesting that the deficiency in the ration of vitamin A was not great enough to produce the acute form.

In connection with the question of scurvy in rabbits, the authors  
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fed these animals a ration presumably deficient only in vitamin A. Butter-fat was added to the ration and in some cases 1 gm. per day of orange peel, dried at room temperature, to furnish vitamin C. In no case were the authors able to bring a rat to maturity on this semi-purified ration, plus butter-fat and orange peel. A similar failure on the part of rabbits to grow on a purified casein ration so supplemented as to be satisfactory for the rat was also demonstrated by the authors. Such rations, without the orange peel, are perfect as far as the nutrition of the rat is concerned but are not satisfactory for the rabbit. The authors attempted to produce scurvy in the rabbits by feeding a ration devoid of vitamin C and known to produce scurvy in guinea-pigs very quickly, but it was observed that this ration failed to produce scurvy in rabbits. Following nutritional experiments with pigs on a diet deficient in vitamin A, the authors are inclined to class the pig with the rat in that it probably requires less vitamin A than the rabbit.

In their preliminary experiments with chickens, the authors have so far been unable to produce xerophthalmia in them. In fact, the development of leg-weakness in the younger chicks has complicated the experiments, but a discussion of this symptom of malnutrition will be presented later by the authors.

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**Vitamin Studies. IX. The Influence of the Diet of the Cow upon the Quantity of Vitamins A and B in the Milk.**

*Cornelia Kennedy and R. A. Dutcher, J. Biol. Chem., 50:339, Feb., 1922.*

In the experiments on rats described in this paper, two types of cows' milk were employed, one produced on a ration typical of that used on some farms during the winter season and known to be deficient in its vitamin content, and a second representing that produced on a ration carrying ample amounts of vitamins A and B. Each milk was fed so as to show in as nearly a quantitative manner as possible its content of vitamins A and B. A 10 or 15 c.c. quantity of the milk was fed daily to each of the 6 normal rats of each group. The authors have plotted their results as growth curves demonstrating the possibility of growth on low and high levels of each milk. From the data thus tabulated the authors conclude that the presence of vitamins A and B in cows' milk is entirely dependent upon their occurrence in the ration. Stall-fed cows will produce a milk rich in vitamins provided their ration consists of a proper combination of grains and leafy foods. A vitamin-rich milk is not necessarily correlated with access to pastureage. The authors also remark that 10 c.c. per day of either winter or summer milk is adequate to furnish either vitamin A or B to a rat provided the ration of the cow carries each in amounts adequate to meet her requirements, but 5 c.c. of the same milk that produced normal growth when used on a higher level does not furnish enough of either vitamins A or B to meet the requirements of growing rats. The effect of the vitamin is not necessarily one of appetite stimulation but rather a stimulation of metabolic processes which promote growth.

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A Study of the Effect Produced on the Composition of Milk by the Administration of Certain Inorganic and Organic Substances.

*W. Denis, Warren R. Sisson, and Martha Aldrich, J. Biol. Chem., 50:315, Feb., 1922.*

The effect produced on the composition of the milk and the blood of goats by the gastric administration of urea and of calcium chlorid was studied. The analytical methods used were as follows: For milk the urea content was determined by the urease method according to the technic described by Denis and Minot the calcium content was determined by a modification of Lyman's method. For blood the urea was determined by the method of Folin and Wu and the calcium was determined by the method of Lyman. An appropriate amount of the substance whose absorption was to be studied was dissolved in about 300 c.c. of water and poured down the animal's throat. In one instance, as a further check on the results obtained by gastric administration, 1.87 gm. of calcium chlorid was administrated intravenously in a volume of 75 c.c. Tables I, II and III in the article show the effect on the blood and milk of administering large doses of urea—a marked increase of urea nitrogen over normal resulting in both. An attempt of the authors to influence the calcium content of the milk or blood by the administration of large doses of calcium chlorid was unsuccessful, although an increase in the chlorid concentration of the milk and plasma resulted. It is concluded that if the mammary tissue acts as a temporary storage place for certain substances that are not rapidly excreted, both the chlorin ion and urea may be found in increased amounts in the milk when their concentration in the plasma rises to a high level. The different behavior of the calcium ion is due to the fact that calcium cannot be retained in the mammary tissue but is excreted almost immediately by the intestine and kidney.

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Nutrition Experiments on Tadpoles and the Importance of Tryptophan.

*W. Kolmer and Ferd. Scheminzky, Pflüger's Arch. f. d. ges. Physiol., 193:93, Berlin, Dec. 8, 1921.*

From the various researches so far made on the biologic importance of the different proteins in the food, we have learned, in consequence of experiments upon men and other mammals, that a large number of protein substances are necessary for a complete and satisfactory diet. Among these indispensable proteins is tryptophan (indolaminopropionic acid). Thus gelatin has been shown in numerous attempts to be insufficient as an exclusive protein article of diet, being deficient in tyrosin and tryptophan. Newer experiments have demonstrated in a most direct manner the indispensability of tryptophan. Abderhalden has renewed the experimental work with gelatin and shown clearly that on the addition of tyrosin and tryptophan there results a perfectly satisfactory protein food. Since Fürth perfected his method for the detection of tryptophan, at least qualitatively, in the minutest amounts, it was inevitable that other articles of diet shown by this method to be devoid of tryptophan should be investigated as to their biologic value.

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By reason of easy accessibility and great supply of similar individuals, larvae of cold-blooded animals have been selected for experimental material especially suited to this work. Food-stuffs shown by Fürth's method to be tryptophan free (horses' serum albumin, horses' blood corpuscles, lard, rice starch, and combinations of these) were fed to series of 50 tadpoles each; as controls similar animals were used, either without any food at all or with algae within reach. Furthermore, parallel tests were made on animals with and without the addition of yeast. The tryptophan complex promptly set in in the tadpoles, thus showing that this substance is necessary also for the nutrition of cold-blooded animals. The food combinations, even with the addition of yeast (vitamins), seemed not to contain all the elements necessary for normal growth and proper development. From the results obtained it seems that a combination of serum albumin and starch is particularly suitable to sustain life, while a combination of blood cells and starch is particularly suitable for growth.

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**Poultry Fleshaing Investigations. The Utilization of Soy Bean and Corn Proteins as Affected by Suitable Mineral Supplements.**

*D. C. Kennard, R. C. Holder and P. S. White, Am. J. Physiol., 59:298, Feb. 1, 1922.*

In this investigation an attempt was made to ascertain the value of soy bean meal as a constituent of poultry rations with a view to the practical application of the findings to the needs of the poultry fattening industry. The study deals with the following questions: Is soy bean meal deficient in mineral matter to such an extent as to affect its feeding value? If so, what is the nature of the deficiency, what is the most efficient way of overcoming it, and what effect does it have on the assimilation of protein and the storage of fat? The experiments were conducted with birds confined in metal batteries similar to the usual commercial feeding batteries except that they were partitioned into individual compartments 9 in. by 18 in. Barred Plymouth Rock cockerels from standard bred stock were carefully selected for uniformity of size, quality and vigor, from large numbers of birds received by a market poultry dealer. Each bird was weighed at the beginning of the experiment and at the end of the fourth, eighth and fourteenth days. The birds received their feed twice daily in the form of a batter in individual cups so constructed as to prevent all possible waste of feed, thus making it possible to secure accurate daily individual feed records. No water was given the birds except what was added to the dry feed mixture to make it of such consistency that it would pour from one container to another. Three rations were used in the investigation. These consisted of a basal ration,—corn meal, soy bean meal and water; the basal ration plus various salt mixtures; and a ration consisting solely of corn meal and buttermilk (40:60). At the beginning and at the end of the feeding experiment, specimens representative of the unfed and of the fleshed birds were killed, carefully bled, dry picked, and chilled for twenty-four hours in a room at 33°F. After weighing (chilled weight) they were dissected so as to separate the edible from the inedible part, and a composite analysis of the meat, skin and edible

organs was made. From a study of the tabulated results one learns that corn meal and soy bean meal (81:19), the basal ration, supplemented by the essential mineral elements, produced gains in broilers and springs nearly equal to that obtained by the use of a ration of corn meal and buttermilk (40:60), while the basal ration without the mineral supplement proved distinctly inferior. A salt mixture consisting of bone ash, calcium carbonate and sodium chlorid (60:20:20) was the simplest mixture that proved effective in overcoming the mineral deficiency of the basal ration. The optimum amount of the salt mixture to be added to the basal ration seems to be approximately 2% of the dry feed. It appears that the mineral deficiency of the basal ration is not such as to interfere with the storage of fat, but rather accelerates its formation at the expense of protein growth. The increase of flesh produced by the ingestion of the basal ration supplemented by the salt mixture contained 61.38% more protein than that obtained by feeding the basal ration without the salt mixture. The birds receiving the supplemented ration retained 27.38% more of the nitrogen ingested than did those receiving the basal ration alone.

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**The Metabolism of Sulphur. IV. The Oxidation of Cystin in the Animal Organism.**

*Howard B. Lewis and Lucie E. Root, J. Biol. Chem., 50:303, Feb., 1922.*

In this investigation Lewis and Root endeavored to determine some of the factors involved in the oxidation of the sulphur of the cystin molecule in the animal organism. Phenyluraminocystin was prepared from cystin (obtained by hydrolysis of human hair) and phenylisocyanate according to the method of Patten. The recrystallized product showed on analysis results which corresponded closely to the theoretical values for sulphur and nitrogen. The animals used were rabbits which were maintained on a diet of milk, to which cane-sugar was added. A solution of phenyluraminocystin was either injected subcutaneously or fed through a gastric sound. Cystin was administered either as the sodium salt or as the hydrochlorid. The tabulated results show that the sulphur of phenyluraminocystin when administered subcutaneously as the sodium salt was not oxidized in the organism of the rabbit, but was eliminated as extra unoxidized sulphur. Cystin under the same experimental conditions did not increase the unoxidized sulphur content of the urine. When the sodium salt of phenyluraminocystin was fed to rabbits, a limited oxidation of the sulphur fraction of the molecule, resulting in a slight increase in the elimination of sulphate sulphur occurred, although the greater part of the sulphur administered was recovered in the unoxidized sulphur fraction. Since uramino-acids are not broken down in the organism these results indicate that the oxidation of the sulphur of the cystin molecule is connected with the process of deamination or the oxidation of the deamination products.

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The Relative Excretion of Urea and Some Other Constituents of the Urine.

*E. B. Mayrs, J. Physiol., 56:58, London, Feb. 14, 1922.*

The author performed a series of experiments on the excretion of the waste products of metabolism with which the kidney has ordinarily to deal. Anesthetized rabbits were injected with sodium sulphate and urea; anhydrous sodium sulphate and anhydrous  $\text{Na}_2\text{HPO}_4$  with sufficient  $\text{H}_3\text{PO}_4$  to render the solution practically neutral to litmus; creatinin and anhydrous sodium sulphate. A sufficient time after the injection samples of the blood and urine of the animal were examined to determine the concentration ratios for the particular pair of substances. The tabulated results show that no 2 substances were definitely proved to have exactly the same concentration ratio, but sulphate, phosphate, and creatinin differ only slightly in the degree to which their concentrations are raised, and a small relative alteration in their plasma concentrations during the experiment might account for this difference. These 3 substances are concentrated to a considerably greater extent than is urea. Raising the ureteral pressure increases the difference between the concentrations of urea and of sulphate in the urine, by reducing the output of urea more than that of sulphate. The degree of difference between the concentration ratios of 2 substances seems to determine the extent to which pressure affects their relative concentrations in the urine. The author believes this evidence to be, on the whole, more favorable to the theory of reabsorption in the tubules than of secretion, for if the concentration ratios of certain very different substances are so nearly the same it is difficult to suppose that they are secreted independently of each other. It is easier to assume that they are concentrated by removal of water. Similarly, the greater the diffusibility of any of the substances examined the lower appears to be its concentration ratio. It is not easy to see why diffusibility should be a hindrance to secretion, but one can understand why it should aid absorption from the tubules.

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Studies on the Acetonuria Produced by Diets Containing Large Amounts of Fat.

*Roger S. Hubbard and Floyd R. Wright, J. Biol. Chem., 50:361, Feb., 1922.*

Hubbard and Wright undertook a study of diets which produce borderline acetonuria and at the same time maintain unchanged the body weight of the subjects. The diets used were figured from the tables given in Joslin's Diabetic Manual (1919). The intake of carbohydrates and of fat formed, respectively, the sources of 10 and 80% of the calories in the basal diet, and of varying percentages—5 and 85%, 15 and 75%, 20 and 70%—in the other diets studied. An attempt was made to feed each of these diets for a period long enough to determine the level of acetone excretion which corresponded to it, but it was usually necessary to change the more severe diets before such an equilibrium was established. The name antiketogenic has been applied to compounds which furnish glucose or other related compounds with which the acetone body combines. The ketogenic compounds con-

tained in the diets devised by Hubbard and Wright were the fatty acids contained in the fats and the a-amino-acids, leucin, tyrosin, phenylalanin, and possibly histidin which form a part of the proteins. There was probably a molecule of the acetone bodies derived from each molecule of these compounds contained in the diet. The name ketogenic refers to those compounds which give rise, in the progress of metabolism, to aceto-acetic acid. The amounts and source of the anti-ketogenic compounds contained in the diet are uncertain. Glucose and related sugars form one source of these substances. Protein yields glucose when fed to the total diabetic in amounts which vary with the different kinds of food-stuff, and some percentage of the protein should therefore be included with the carbo-hydrate in figuring the total anti-ketogenic intake. In addition there is much data indicating that glycerol yields glucose under some conditions, and so fat, from which glycerol is produced by hydrolysis in the organism, must also be considered as a possible source of antiketogenic compounds. The authors performed a series of 6 experiments in which the effect of diets high in fat on the excretion of the acetone bodies by normal subjects was studied, and the results compared with the mathematical formula devised. As a result of this work the authors conclude that the mechanism which controls the formation of increased amounts of the acetone bodies can be regarded as a molecular reaction or balance between ketogenic substances such as the fatty acids and antiketogenic substances such as glucose. Protein figures as an antiketogenic compound only to the extent of the glucose which it can yield in the organism. Glycerol, when fed as a part of the fat molecule, figures as an antiketogenic compound to which glycerol itself can yield glucose.

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**Influence of Light Rays upon Nuclein Metabolism.**

*Ludwig Pincussen and Karl Momferratos-Flores, Biochem. Ztschr., 126:86, Berlin, Dec. 27, 1921.*

A breaking down of the nuclein metabolism takes place under the influence of light rays. In the present experiments, the influence of other rays, especially of Roentgen rays, was examined, as well as the possibilities of the influence of the nuclein-splitting enzyme of the blood. The destruction of the nucleic acid was estimated according to the optic method of Pighini and Neuberg (changes of rotation in the polarization microscope). The experiment showed that destruction took place insofar as markedly right rotating split-products were thrown off. Apparently, the carbohydrate complex was freed from the nucleic acid. A 2% solution of yeast sodium nucleinate was used. A nitra lamp of 300 candle power was the source of light. The heat rays were absorbed by a layer of water, and the raying took place both without any addition and with the addition of about 2-5% of a sensitized stain. A 5% solution of eosin, a 0.2% solution of 2.7 dichloranthracendisulphacid sodium and a 0.2% solution of methylene-blue were used. The splitting of the nucleic acid, in the above-mentioned sense, is very evident on the addition of eosin, as well as on raying without stains. Sensitizing with anthracen stain, as well as Roentgen rays, are without effect. Nucleic acid may be split by normal serum. In the determination of the ability of the serum to split nucleic acid, as influenced by light

rays, all experiments demonstrated that the fermentation ability of the serum cannot be increased by light or by Roentgen rays. Splitting experiments with the serum of untreated rabbits, as well as with the serum of rabbits treated with different kinds of waves, demonstrated an increase in the splitting ability of the serum. Furthermore, the intermediate metabolism of the different stages of the breaking down of the nucleic acid, especially after sensitization by fluorescent stains, is influenced by the light rays. In this case, the end-products of the nuclein metabolism are different than they would be under ordinary conditions. The breaking down was carried out beyond allantoin and uric acid down to oxalic acid. The quantities of oxalic acid, found after intravenous administration of nucleic acid, uric acid, guanin or xanthin, amounted to 75% of the theoretic value. After oral administration, the increase of oxalic acid was less marked. There was, however, always a higher excretion of oxalic acid in the rayed animals than in the untreated controls. The nucleic acid was dissolved in NaOH and introduced directly into the esophagus; the purin bases and the uric acid were dissolved in piperazin and injected intravenously.

The roentgenization took place at a distance of 5 c.c. from the belly of the animal. All the experiments show that the light rays influence the metabolism of the purin bodies in the form of a further oxidation of the purin bases. The addition of uric acid or xanthin causes in itself an increase of oxalic acid excretion. The quantity of oxalic acid is, however, increased if in addition to these substances, x-rays are applied.

All these experiments indicate, without doubt, that oxalic acid is the chief reaction of the oxydative destruction of the purin bases.

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**The Effect of Intravenous Injections of Sugar upon the Excretion of Lactic Acid, the Blood Sugar and the White Blood Corpuscles.**

*Waclaw Moraczewski, Biochem. Ztschr., 125:49, Berlin, Dec. 8, 1921.*

Investigations were conducted to determine the behavior of the blood sugar and the excretion of levulose and dextrose, when injected simultaneously. The following experiments showed that only levulose, not dextrose, caused chills; the chills observed with inverted sugar are attributed to levulose.

The blood sugar was determined by Bang's method. Immediately before the injection of the sterilized dextrose or levulose solution, the number of the red and white corpuscles was determined; one hour after the injection the red and white corpuscles were again counted and the blood preparations were made. The polynuclears, small lymphocytes and large mononuclears were counted; the eosinophils were disregarded and the transitional forms were counted with the large mononuclears. In the urine, the phosphoric acid was determined with uranium acetate by the use of cochineal as indicator and the lactic acid was determined by the Fürth-Charnas-Schneyer method: 50 gm. dextrose were dissolved in 50 c.c. distilled water, filtered and sterilized before it was injected. The tests were tried on anemic, syphilitic, tuberculous, arthritic, alcoholic and normal persons; in some cases phlorizin, adrena-

lin, deuteroalbumose, salvarsan, collargol and dextrin were also administered. The results were as follows:

Under the supposition that lactic acid is the expression of sugar combustion it may be said that with an increased temperature or with an abundant administration of carbohydrates there is always a more marked accumulation in the blood and a correspondingly greater excretion of lactic acid in the urine. There seems to be no parallel between the excretion of phosphoric and lactic acids. An abundant excretion of lactic acid was demonstrated without the phosphoric acid being increased and vice versa.

The slight amount of lactic acid in typhoid cases is always attributable to the very low intake of food.

In fevers, the lactic acid as well as the blood sugar is increased; so that an increased mobilization and combustion of sugar can be assumed. The increased excretion of lactic acid after the administration of carbohydrates is especially noticeable on the giving of levulose in the diet and is not so marked with the giving of dextrose. The effect of intravenous injections is still more prominent: in this case the dextrose produces a hardly demonstrable increase of lactic acid, but the levulose, on the other hand, produces a marked increase. After feeding dextrose the lactic acid increased from 50 to 54 mg. and after a like amount of levulose there was a rise from 50 to 100 mg. Dextrose injected intravenously increases the lactic acid from 60 to 80 mg. and from 117 to 170 mg. respectively; the same amount of levulose causes an excretion of 200-600 mg. per day. The rule holds that those cases which show an abundant excretion of lactic acid respond with a more abundant excretion of lactic acid to levulose injection, but those organisms which produce a slight amount of lactic acid also produce the slightest increase after the injection of levulose. Diabetes usually showed increased lactic acid values in the urine, but even in healthy persons high values for lactic acid were also found. In anemics, where oxidation is slight, only a slight increase was observed. In spite of the increased temperature, deutero-albumoses, as well as collargol or salvarsan do not produce an increased amount of lactic acid, but phlorizin and adrenalin, on the other hand, do produce an increased excretion of lactic acid, which speaks for a mobilization of sugar by phlorizin. With injections of dextrose and levulose the blood sugar values increase, and that all the more, the slower the oxidation or assimilation of the organism. Leukemic, anemic and febrile patients generally show a greater increase of blood sugar values after an intravenous injection.

Immediately after a meal there is always an increase of the blood sugar. The conclusion that levulose is more assimilable cannot be drawn from these experiments and what is more, the grape sugar seems not to be subject to oxidation and shows a tendency to the deposit of glycogen; this conclusion is valid on the supposition that the lactic acid excretion serves as the expression of combustion. Because of its structural formula or its poor assimilation, levulose is undoubtedly a pronounced former of lactic acid. The temperature after injections is comparatively higher in febrile cases than in those with normal temperature. Fever appeared after injections of both levulose and dextrose. After injections of lipoid and deuteroalbumoses, the variations of temperature were slight; after dextrose, salvarsan and collargol there were no disturbances at all. In fevers, there were variations in the number

of the white blood corpuscles: in tuberculosis and acute diseases, where an increase of the white blood corpuscles does occur, the variation is considerable; with torpid individuals, where also the temperature shows no marked increase, the white blood corpuscles vary little. In cases where no lowering of the white corpuscles occurs, the small lymphocytes show an increase, probably because in these cases the lymphatic system shows a marked development or irritability. The large mononuclears are increased after the injection of levulose but are increased after an injection of lipoid.

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**Paradoxic Sugar Metabolism under the Simultaneous Influence of Pilocarpin and Adrenalin. (Dissimilatory Reversal).**

*R. Vogel und A. Bornstein, Biochem. Ztschr., 126:56, Berlin, Dec. 27, 1921.*

Adrenalin and pilocarpin are toxins which produce contradictory effects on most organisms. The first stimulates the endings of the sympathetic nerves and the latter those of the vagus or parasympathetic nerves. These two kinds of nerves innervate most of the organs in an antagonistic manner. It is, therefore, striking that pilocarpin, similar to adrenalin, causes an increase of sugar in the blood, while at the same time a consumption of the glycogen of the liver takes place. An accordance of the action seems apparent. In using both toxins simultaneously, the effects should be added. Several experiments were undertaken to verify this expectation. In order to obtain a correct idea of the conditions, adrenalin alone, pilocarpin alone, and finally both toxins together were used, the amounts being varied within certain limits. The blood was taken from the vein of the ear and the sugar determination was made after Bang's method. The experiments were carried out with small quantities of adrenalin and pilocarpin, and then increased with medium quantities 0.19 mg., 0.61 mg. per kilo animal-weight. In a few cases pilocarpin was substituted by physostigmin. The experiments show that either pilocarpin or adrenalin, when given separately can increase the blood sugar, but if given simultaneously cause a mutual inhibition. This forces the conclusion that pilocarpin glycemia is different from adrenalin glycemia; we should have otherwise a simple summation of effects. In reality, we have no immediate change of the blood sugar after the simultaneous injection of adrenalin and pilocarpin. In other words, the pilocarpin nullifies the adrenalin action and the adrenalin nullifies the pilocarpin action on the blood sugar. These observations are in accord with the theory of a sympathicus sugar and a parasympathicus sugar; there is no need of a summation when the points of attack of the toxins are so different.

It has often been shown in the functions of animals that two toxins can give a similar result, but that if they are given simultaneously, they will counteract each other; after administration of ergotoxin as well as of adrenalin the effect upon the blood pressure is inhibited. The phenomenon is called "motor reversal." Correspondingly, the effect of pilocarpin and adrenalin as described may be called "dissimilatory reversal."

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**The Decomposition Products of Cholesterin in Animal Organs. Accompanying Substances of Blood Cholesterin. X.**

*I. Lifschütz, Hoppe-Seyler's Ztschr. f. physiol. Chem., 17:201, Berlin, Dec. 27, 1921.*

In the quantitative estimation of cholesterin in liver fat the values obtained by precipitation with digitonin (gravimetric analysis) and those obtained by spectrometry of the cholesterin color reaction are found to agree completely. This is not the case with blood fat; spectrometry yields considerably higher values than the gravimetric digitonin method, for the following reasons: Liver fat does not contain any substance precipitable with digitonin except cholesterin, nor any substance besides cholesterin which reacts with aceto-anhydrid-sulphuric acid (cholesterin reaction). Therefore, both methods yield the same cholesterin values. Blood fat, on the other hand, contains, in addition to cholesterin, considerable amounts of an accompanying substance—oxycholesterin—of which not all but merely a portion is precipitated by digitonin. But, as oxycholesterin also gives the cholesterin reaction, like cholesterin, the digitonin method will indicate not only total cholesterin, but also a part of the oxycholesterin. In spectrometry, however, both cholesterin substances are wholly represented in the spectrum and will, therefore, be included in the cholesterin value obtained by this method. That is, spectrometry determines the sum of the cholesterin and oxycholesterin values, whereas the digitonin method yields values too low for the sum of both cholesterin substances but too high for cholesterin alone. This shows how important a knowledge of the so-called accompanying bodies of cholesterin is in the analysis of that substance, particularly in the analysis of blood cholesterin.

The author's experiments yielded 2 groups of bodies accompanying blood cholesterin, one of which forms double compounds with digitonin, while the other does not combine with the latter. Both groups are pronounced cholesterin derivatives. The second group of accompanying substances not precipitated by digitonin consists of at least 3 cholesterin oxids, namely: (1) an oxid proved by the direct acetosulphuric acid reaction to be very similar to true oxycholesterin, either isomeric with it or derived from it by further oxidation; the color and spectrum of its oxycholesterin reaction solution, shaken with chloroform, does not reach the substratum, but is not precipitated by digitonin; (2) a probably neutral oxid derived from the oxidized cholic acid, the oxycholesterin reaction of which, after treatment with chloroform, falls to the substratum; and (3) a further cholesterin oxid, which like cholic acid, gives no direct reaction but does give the "latent" oxycholesterin reaction very clearly as regards color and spectrum. After treatment of this reaction solution with chloroform, the color and absorption spectra of this substance—like cholic acid—fall to the substratum. Besides oxycholesterin reactions with acetosulphuric acid, both groups of the afore-mentioned accompanying substances of blood cholesterin including those not precipitable by digitonin, give the familiar Liebermann cholesterin reaction with aceto-anhydrid-sulphuric acid, with great intensity and in all colors and spectral absorptions, like cholesterin itself. Hence it cannot be questioned that the total content of unsaponifiable substances in blood fat, which are insoluble in water, consist exclusively

of cholesterin substances and they have, in fact, all been produced artificially from pure cholesterin.

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**Metabolism of Calcium in Normal Man.**

*G. E. Puxeddu, Riforma med., 38:98, Naples, Jan. 30, 1922.*

The author has practiced experiments upon three 30-year-old persons in apparent health, subjecting them for four days to a mixed diet consisting of bread, rice, butter, milk, spinach, oil, eggs, meat and water, containing in all 4.53 gm. Ca O. He then began to determine the amount of calcium eliminated, continuing the above diet for two days, adding for the next two days 2 gm. calcium lactate, and finally adding for two more days 3 gm. calcium lactate. A daily mean elimination of 53.86% of the calcium introduced was noted, 31.85% by the feces, and 22.01% by the urine; hence the mean retention was 46.14%. At the same time there was seen an increase in the calcium content of the blood. This increase has limits beyond which either disturbances are produced, or there arises a crisis of discharge. The crisis of discharge comes on all the more quickly if the calcium has been introduced into the organism in a more dissociable form; for example, in the form of calcium chlorid.

The calcium of the blood increases within more physiologically compatible limits with the administration of alimentary calcium than with that of calcium salts, which latter seem at a certain point to favor its decrease.

The elimination of calcium by the feces is ordinarily greater than that by the urine, according to what other scholars have stated, but the difference is still more marked in those experiments in which calcium lactate has been added to the diet. It is possible that in this case the calcium is not eliminated passively as refuse of the intestine, but goes through the circle indicated by Voit between the small intestine (absorbment) and the colon (elimination). Finally, in a diet too rich in calcium, the percentage of elimination by the urine is higher by more than twice as much than the maximum percentage found registered for ordinary diet (5 to 10% of the calcium introduced).

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**The Metabolism of Pigment.**

*Fromholdt and Nervesoff, Biochem. Ztschr., 125:149, 153, Berlin. Dec. 8, 1921.*

The elementary formula  $C_{16}H_{18}N_2O_8$  is accepted for bilirubin but the pigment analyzed originated exclusively from gall-stones. Experiments were conducted to see if the same elementary formula results if bilirubin from various sources is produced and analyzed. Bilirubin from a fresh pig gall-bladder, from mixed urine of several cases of icterus, and from the urine of 2 different cases of cirrhosis, liver and pancreatic cancer were examined. The carbon and hydrogen were estimated by the micromethod of Pregl, the nitrogen by Kjehldahl's method, and erythrosin was used as an indicator instead of methyl-red. The analyses showed that in the various cases formerly reported, the bilirubin always showed the same elementary construction. A large

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amount of a green pigment was found as a by-product in cases of icterus and it is very likely that the color of icteric urine is principally due to other pigments.

A second paper is based on observations on experimental icterus produced through mechanical closure of the bile-duct by ligation and by various poisons. Injection experiments were made with bilirubin for the purpose of securing pigmentation of the tissues. In the preliminary experiments, in which too much pigment was used, it was shown that 0.2 gm. bilirubin injected into rabbits was lethal. The animals refused food, and diarrheas and convulsions resulted; when urine was excreted, it contained albumin and sometimes blood. Therefore rabbits were injected with only 0.1 gm. bilirubin and dogs with not more than 0.6 gm. A true icterus was not produced in the animal experiment, but usually there was a slight subicterus or a yellow tinge of the tissues. The biliary pigment reached the urine only in the dogs. If the bilirubin injection is repeated several times in one day, a pronounced urobilinuria results, but rabbits never show bilirubin in the urine. Urobilin was demonstrated with Neky's test and its chromogen with Ehrlich's reagent. There seems to be a relationship between bilirubin in the plasma and urobilin in the urine. Special tests must decide whether that alone is the cause of urobilinuria or whether other factors are effective.

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**The Nomogram as a Means of Calculating the Surface Area of the Living Human Body.**

*W. M. Feldman and A. J. V. Umanski, Lancet, 202:273, London, Feb. 11, 1922.*

The nomographic method is described as affording a more simple means than is offered by the Du Bois curves and the Meeh formula for calculating the surface area of the body. The nomogram is an alignment chart, in which 3 parallel lines represent the 3 variables, weight, height and surface area. Each line is notched, as a scale, for its unit values. Taking the formula  $S = 71.84, W^{0.425} H^{0.725}$ , S is the surface area in sq. cm., represented on a line in the center of the chart; W is the weight in kg., represented by a line to the left of and parallel with the surface line; H is the height in cm., represented by a line to the right of and parallel with the surface and height lines. A straight line drawn from the figure which equals the subject's weight, on line W, to the figure representing his height on line H, passes through the figure or notch on line S which equals his body surface area. If the subject is 24 kg. in weight, 110 cm. in height, a line drawn from 24 on line W to 110 on line H will pass through the notch on line S which reads the surface area as 8375 sq. cm.

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**Energy Expenditure in Sewing.**

*C. F. Langworthy and H. G. Barott, Am. J. Physiol., 59:376, Feb. 1, 1922.*

A series of 43 experiments was made with the same subject, under conditions that were kept as uniform as possible, except as regards bodily activity, which was varied according to the nature of the  
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individual experiments. In order to determine the energy required for a specific task the energy expenditure during the period of such work was compared with the expenditure during a period of complete rest and the difference between the two was taken to represent the energy required for the task itself. The subject, a 28 year old female, entered the calorimeter at 10 a. m. The experimental measurements were begun between 11:00 and 11:30 a. m. and continued for two hours. The tabulated results record the energy expended by a woman hemming by hand on various materials and at different speeds and doing similar sewing on a machine driven by foot power and by electricity. Little variation is shown in the energy required for hand hemming on fine handkerchiefs, cotton sheets, 8-ounce cotton duck, and army blankets, the energy required for the actual sewing running between 5.5 and 5.8 calories per hour except in the case of army blankets where it was only 4.3 calories. When the speed was increased, the energy output increased proportionately. Hemming sheets on a foot-driven machine required about 6 times as much energy per hour as doing the same work by hand, but the energy used per meter of sewing was hardly one-half as great. When an electrically driven machine was used, the energy required per hour was not quite twice that used for hand sewing and about one-fourth that for the foot-driven machine; the energy per meter of sewing was about one-fifth of that measured on the foot-driven machine and less than one-tenth that of hand sewing.

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### An Explanation for the Increase in Oxidation Brought About by Muscular Work.

*W. E. Burge and J. M. Leichsenring, Am. J. Physiol., 59:290, Feb. 1, 1922.*

The authors have previously determined that whatever increases oxidation in the body, the ingestion of food, cold baths, exposure to low temperatures, etc., produces an increase in catalase, an enzyme possessing the ability to liberate oxygen from hydrogen peroxid, and that whatever decreases oxidation, narcotics for example, produces a decrease in catalase. In seeking an explanation of the increase in oxidation brought about by physical work, the authors naturally studied this enzyme. The animals used were rabbits which were exercised by running. Catalase determinations of the blood of the jugular vein were made immediately before and after the exercise. The determinations were made by adding 1 c.c. of diluted blood to 150 c.c. of neutral hydrogen peroxid in a bottle and taking the amount of oxygen liberated in ten minutes as a measure of the catalase content of the blood. The charted results show that moderately severe muscular exercise increases the blood catalase, and with subsequent rest this returns to normal. The increase in oxidation brought about by muscular work is attributed to the increase in catalase, and the decrease in oxidation with subsequent rest is attributed to the diminution in this enzyme, in the opinion of the authors.

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**Renal Blood-Flow and Glomerular Filtration.**

*E. B. Mayrs and J. M. Watt, J. Physiol., 56:120, London, Feb. 14, 1922.*

If the blood-flow through the kidneys in man is taken as 2500 liters in twenty-four hours and the average urea content of the blood as 0.2 gm. per liter, the total amount of urea which passes through the renal vessels each day is 500 gm. However, the daily excretion of urea is only about 30 gm. or 6% of the quantity supplied to the kidney by the blood stream. But since the blood urea is distributed equally between plasma and corpuscles and the time spent by each unit of blood in the renal circulation is insufficient to allow an appreciable amount of diffusion to occur, it is evident that the relative proportions of plasma and corpuscles must be considered when determining how much urea is actually available for excretion. If one assumes that half the total volume of blood consists of plasma it follows than 12% of the available supply of urea is eliminated. This means that 88% of the plasma has not come into effectual contact with the renal cells, and is altered in its passage through the kidney only in so far as it is diluted with the fluid that has come into such contact. To verify such a conclusion the authors investigated the above relationship in rabbits, determining (1) the volume of plasma which circulates through the kidney in a given time (2) the total amount of sulphate contained in this plasma, and its concentration. Sulphate was used for measurement since it is more efficiently eliminated than urea. (3) The quantity of sulphate which escapes in the urine during the same period. The tabulated results show that the glomerular filtrate, or the proportion of plasma which comes into efficient contact with the excretory cells, is from 20 to 25% of the whole plasma circulating through the kidney, but this proportion is subject to wide variations.

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**The Action of Minute Doses of Adrenalin and Pituitrin on the Kidney.**

*A. N. Richards and O. H. Plant, Am. J. Physiol., 59:191, Feb. 1, 1922.*

In order to determine whether the striking coincidence of vasoconstriction and vasodilatation within the excised kidney, when perfused with blood containing pituitrin or adrenalin, could be demonstrated in the intact animal, experiments were performed on anesthetized rabbits, cats and dogs, which had been made diuretic before the experiment. A tracheal cannula was inserted and the arterial blood pressure recorded by a mercury manometer attached to the carotid artery. Intravenous injections were made through a cannula in the jugular vein. The vagus and splanchnic nerves were cut. The right kidney was ligated and in some experiments excised. Both suprarenal veins were ligated. After ligation of the abdominal aorta below the origin of the left renal artery, the inferior vena cava was prepared for the Barcroft-Brodie method of estimating blood flow through the kidney. The left kidney was put into a gutta percha oncometer, a small Brodie bellows being used to record changes in its volume. A cannula was inserted into the left ureter and urine flow from it registered by a drop recorder. In the results, which are recorded graphically, neither the

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extent of diuresis, the expansion of the kidney nor the diminution in blood flow, taken individually, is impressive; their coincidence, however, is very impressive and the authors believe that it constitutes evidence that these substances in high dilution exert a selective constriction of the efferent vessel in comparison with the afferent. The experiments bear upon the problem of glomerular regulation of urine formation.

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**Urine Formation in the Perfused Kidney. The Influence of Alterations in Renal Blood Pressure on the Amount and Composition of Urine.**

*A. N. Richards and O. H. Plant, Am. J. Physiol., 59:144, Feb. 1, 1922.*

For each experiment 2 rabbits were used, one as the subject of the experiment, the other supplying blood for the perfusion. The operation on the first rabbit was as follows: Cannulas were inserted, one into the trachea for artificial respiration, one into each carotid artery (for record of blood pressure and for supplying blood to the perfusion pump respectively), and one into an external jugular vein for injections. The gastro-intestinal tract was removed after successive ligation of the celiac axis, superior mesenteric and inferior mesenteric arteries and portal vein. The vessels of the right kidney were ligated. In some of the experiments the splanchnic nerves on both sides were divided. The abdominal aorta was ligated about 1 in. below the origin of the left renal artery, and lumbar arteries issuing between the level of the renal artery and the ligature were tied. The inferior vena cava was similarly ligated at the same level and, after clamping, a cannula was inserted into it and another into the aorta pointing toward the heart. These cannulas were connected with each other and with the output tube of the perfusion pump by means of a small 4-way glass tube, the fourth arm of which served for the introduction of the bulb of a small thermometer into the perfusion stream. By this means blood could be driven from the pump either into the cava or into the aorta. When the operation on the first rabbit was finished, the other rabbit was bled from the abdominal aorta; 12 to 15 c.c. of blood were collected in a dish containing 130 to 150 mg. hirudin. After thorough stirring it was filtered through cotton and slowly injected into the vein of the first rabbit. The rest of the blood of the second rabbit was mixed with 70 mg. of hirudin, filtered and used for filling the pump. Then, with a rabbit prepared for perfusion whose blood was incoagulable and with the pump filled with hirudinized blood, the reservoir which constituted the intake of the pump was connected with the animal's carotid artery. The outlet of the pump was connected with the 2 cannulas, one in the inferior cava, the other in the abdominal aorta. With the clamp on the cava loosened the pump was started and at the same time a clamp on the carotid opened to such an extent as was necessary to keep the level of blood in the pump reservoir constant. The animal was then bleeding into the pump at the same rate as that at which the pump was injecting blood into the animal's body; in this way the blood in the pump and connections was thoroughly mixed with that in the animal's body. At a given signal the clamp on the cava was

closed, that on the aorta opened, and the ligature on the aorta above the left renal artery tied tightly. Then the pump was driving blood, received from the animal's carotid, through the vessels of the left kidney via the aorta; at no time was the circulation through the kidney interrupted. In some instances no interruption in urine flow occurred when the artificial circulation was substituted for the normal. Hürthle membrane manometers were used to register the carotid pressure of the animal and the perfusion pressure from the pump. Urine flow was measured by noting the position of the meniscus of urine in a long graduated cannula tied into the left ureter, and held nearly horizontally. Blood flow through the kidney was measured by temporarily diverting the blood from the carotid into an alternate reservoir and then recording the time required for the pump to lower the level of blood in the reservoir from one graduation to another etched on the reservoir. (A diagram of the arrangement of the perfusion system is shown in the article.) Urine samples obtained throughout the course of an experiment were examined for chlorids, urea and creatinin. The tabulated results show that changes in perfusion pressure induced by splanchnic stimulation, by introduction of adrenalin and nitroglycerin, by compression of the renal vein and by stimulation of the medulla are accompanied by parallel changes in the rate of urine elimination. The authors believe such results constitute direct evidence in support of the filtration hypothesis of glomerular function.

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**Urine Formation in the Perfused Kidney. The Influence of Adrenalin on the Volume of the Perfused Kidney.**

*A. N. Richards and O. H. Plant, Am. J. Physiol., 59:184, Feb. 1, 1922.*

In this work excised kidneys from the rabbit and dog were placed in an oncometer and were perfused by means of the pump used in the experiments described in the preceding paper. Hirudinized blood from the same animal was used as perfusion fluid; no attempt was made to establish the perfusion current without interruption of the circulation, though it was clearly desirable that such interruption be short. As a result of the interruption in the circulation no urine was formed in the experiments; hence expansion of the kidney from the formation of urine within it in these experiments need not be considered. The graphic results show that the addition of a small amount of adrenalin to the perfusing blood caused a rise in perfusion pressure and swelling of the kidney. Since this coincidence of vasoconstriction (manifested by rise of perfusion pressure) and vasodilatation (as shown by increase in kidney volume) does not occur in the leg when its vessels are perfused in the same manner, it must be attributed to the arrangement of vessels existing in the kidney and not in the leg. The experimental results are interpreted by the authors as evidence that the vas efferens is constricted by adrenalin with consequent rise of intraglomerular pressure and distention of the malpighian bodies. The results also explain the diuresis caused by adrenalin.

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**Muscle Energy.**

*Otto Meyerhof, Klin. Wchnschr., 1:230, Berlin, Jan. 28, 1922.*

In muscle, the chemical energy arising from the oxidation of food is transformed into mechanical work. On stimulation of the muscle, thermo-electrical measurements demonstrate the production of heat, a part of which is transformed into work and a part into elastic changes of tension in the muscle. Lactic acid plays an important part in these chemical processes. This accumulates when the muscle contracts so that the muscle becomes exhausted, and it disappears again when acted upon by oxygen so that the muscle is restored. Increased oxygen consumption follows muscle contraction. The production of heat by the stimulated muscle takes place in 2 phases; half is set free at the moment of contraction, the other half several seconds after contraction, yet only in the form of oxygen, as a restorative heat corresponding to the storing of a supply of potential energy. Relations have been shown between heat production and lactic acid production. The prevailing opinion has been that lactic acid does not develop from muscle glycogen, but Meyerhof has shown in recent experiments that glycogen is the only source of lactic acid and that phosphate is indispensable as hexos phosphoric acid is an intermediate carbohydrate in the production of lactic acid, the spontaneous breaking down of which is inhibited by the presence of phosphorous. In the resting period the author shows that there is retransformation of lactic acid into glycogen by way of a peculiar reaction. The ordinary oxygen respiration of the muscle takes place at the expense of the carbohydrate and lactic acid develops from the glycogen, but only a part of it is oxidized while 2/3 to 3/4 of it is retransformed into carbohydrate. When oxygen is removed lactic acid accumulates. Similar processes take place in alcoholic fermentation in which there is the same coferment which appears in the muscle and is involved in the catabolism of carbohydrate.

The processes in respiration and fermentation are closely related and both may be hastened by sodium arsenate. The significance of lactic acid as a shortening substance in muscle is shown by thermochemical methods through the quantitative relations between muscle tension, the amount of lactic acid formed, and the heat conditions. Recent studies of temperature of contracting muscle have shown that the first half of heat production is divided into 3 stages corresponding to increasing tension, maximum tension and relaxation, while the second half or restorative heat follows a few seconds later. Meyerhof attributes relaxation heat to reactions between lactic acid and muscle protein.

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**The Reaction of Resting and Active Muscle.**

*A. D. Ritchie, J. Physiol., 56:53, London, Feb. 14, 1922.*

The author measured the difference of electric potential between a resting and an active muscle by means of manganese dioxide electrodes. These electrodes, which are sensitive to hydrogen-ion concentration, qualitatively at least, consisted of pointed platinum wires which were coated with electrolytically deposited manganese dioxide before each experiment. A sciatic-gastrocnemius preparation was dissected from a frog and arranged so as to avoid movement on stimulation. The

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preparation was set up in a moist chamber, the nerve hanging in air between the stimulating electrodes and the muscle insulating the electrodes. The other gastrocnemius muscle, without its nerve, was hung in contact with the first. The points of the electrodes were inserted 1 or 2 mm. into the depths of the muscle and connected with a potentiometer. Any electromotive force which existed between them initially was balanced up and then one of the muscles was stimulated through its nerve. After eliminating possible sources of error the author noted that no alteration in the electromotive force between the muscles could be observed as the result of stimulating one of them with 100 maximal induction shocks of a few seconds' tetanus. When a tetanizing current was switched on and off there was no corresponding steady change of electromotive force. The author concludes that electrometric observations indicate that there is no appreciable change in the hydrogen-ion concentration of frog's muscle during moderate activity.

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**The Maximum Work and Mechanical Efficiency of Human Muscles, and Their Most Economical Speed.**

*A. V. Hill, J. Physiol., 56:19, London, Feb. 14, 1922.*

In this paper the author deals (1) with experiments by which the maximum work performed by human muscles in a single voluntary contraction may be determined; and (2) with the various factors affecting the work done in, and the mechanical efficiency of, muscular movement in man. The maximum work device consisted of a heavy fly-wheel to provide the inertia against which the muscles had to work. Flexion of the arm was employed in such a way that only the biceps and brachialis anticus muscles were involved. The subject, using only these muscles, pulls the end of a string which is wound around one of the pulleys of the fly-wheel. The speed of rotation is measured by a hand tachometer and the energy developed, after preliminary calibration, from the reading of the tachometer. Variation of the equivalent mass of the fly-wheel is obtained by winding the string round one or other of the different-sized pulleys of the fly-wheel. The experiments were made on a variety of individuals and the results recorded graphically as curves. From a study of these curves one observes that, in all subjects, the greater the equivalent mass the greater the work done, the work increasing rapidly at first with equivalent mass and then more slowly, but continuing to increase up to an equivalent mass of over half a ton. Hill's explanation is that the more rapidly a muscle shortens, the more the potential energy developed in it on stimulation is wasted in the passive and viscous processes associated with the change of form. Only by allowing a passively-stretched muscle to shorten infinitely slowly can the full tale of potential energy be obtained from it, and what is true of the inactive muscle under the tension of external origin Hill believes is almost certainly true of the active muscle under the tension of its own contraction.

The author also determined the relation between the work done and the distance pulled in a single contraction, using various loads. The ordinates (of the chart used to tabulate the results) refer to the work done expressed in kilogram-meters. The abscissa represents the pull in centimeters. The resulting curves demonstrate that the slower the con-

traction the greater the work done. This does not mean that the slower the contraction the more efficiently it is carried out, using the word "efficiency" as denoting mechanical efficiency, the ratio of work done to energy degraded in doing it. The more prolonged contraction necessarily involves a greater degradation of energy in the physiological processes necessary to maintain the contraction, and this factor rapidly neutralizes the advantage of obtaining more work from the more prolonged contraction.

By means of very detailed mathematical formula the author discusses and demonstrates the mechanical efficiency of muscle.

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**The Physiologic Significance of the Variable Permeability of the Investing Sheaths of Muscle Fibers.**

*Gustav Embden and Erich Adler, Hoppe-Seyler's Ztschr. f. physiol. Chem., 118:1, Berlin, Jan. 12, 1922.*

It is assumed that muscular activity is related to increased elimination of phosphoric acid by the kidneys and that the muscle secretes the acid. In order to test this assumption, muscles were suspended in measured Ringer's solution which was then examined for phosphoric acid at definite intervals. In this way it was possible to show that living frog's muscle gives off much more phosphoric acid to the surrounding liquid during work than while at rest. As there was also an apparent relation between fatigue and the amount of eliminated phosphoric acid, experiments were carried out with this in mind.

The gastrocnemius of the decapitated frog was prepared, weighed and suspended between platinum electrodes in Ringer's solution. Oxygen was repeatedly passed through the latter. It was found that the gastrocnemius gave off no detectable phosphoric acid to the solution during several periods of rest lasting twenty and thirty minutes. This having been determined the muscle was stimulated faradically. The period of work was followed by one or more periods of rest of equal length. Phosphoric acid was estimated by Pouget and Chouchak's method; with the reagents (3 parts nitromolybdenic acid and 1 part strychnin solution) clouding took place, which was compared. Up to 0.0003 mg. anhydrous phosphoric acid was detected by this method. A series of experiments was then made on the elimination of phosphoric acid during rest and work respectively, which showed that the gastrocnemius of the living frog, after repeated washing in Ringer's solution, does not give off any detectable amount of phosphoric acid during definite periods of rest. The elimination of phosphoric acid ceases some time after the cessation of work and finally disappears entirely. If the muscle be stimulated elimination of phosphoric acid is increased. Regarding the mechanism of the separation of phosphoric acid it is possible that the permeability of the membrane-like investing layers between the muscle fibers and the Ringer's solution has been increased, or that the osmotic pressure increases the amount of inorganic phosphoric acid in the muscle interior. Under stimulation of equal intensity the more rapid single contractions of the nonfaradized muscle are attended by greater elimination of phosphoric acid than the slower contractions of curarized muscle. The experiments also demonstrated that more pronounced muscular fatigue is attended by increased phosphoric

acid elimination and that muscular recovery goes hand in hand with renewed reduction of phosphoric acid separation. If only slight fatigue ensues during stimulation of the muscle the increase in phosphoric acid elimination disappears quickly after the contractions cease. If the muscle becomes nonirritable to a strong stimulus for a long period, greatly increased phosphoric acid elimination is observed as long as nonirritability persists. In conformity with the fact that irritation in air leads to quicker and more pronounced fatigue the elimination of phosphoric acid by a gastrocnemius stimulated directly and indirectly in air is considerably greater than in a similar gastrocnemius stimulated simultaneously and in the same circuit in Ringer's solution. The elimination during fatigue can not be due to increase of intrafibrillar phosphoric acid. Everything points to the increased elimination of phosphoric acid by the fatigued muscle as the expression of increased permeability of the muscle fibrils. With gradually increasing muscular recovery the elimination of phosphoric acid diminishes and when the original degree of irritability is reestablished it sinks to the minimal rest values. Impending rigor mortis, or death of the muscle, is recognized early by a great increase in phosphoric acid elimination. This, the same as a part of the fatigue phenomena, is explained by the gradual loss of the capacity for alteration of the investing sheath in the sense of a loosening. In accordance with this all those processes are included under the term of recovery which are capable of restoring the capacity for alteration of the investing sheath. There exist a series of action on muscle which, without producing contraction, diminish its irritability; to these belong potassium paralysis, alterations by true narcotics, as well as the paralysis after prolonged action of sucrose solution. It is probable that one or other of these paralyses act by diminishing the capacity for alteration of membrane-like investing layers under an increase of the latter's permeability. And, in accordance with this, the suspension of the muscle in isotonic sucrose solution produces greatly increased phosphoric acid elimination corresponding to the gradually supervening paralysis. The more that irritability diminished the greater was the elimination of phosphoric acid. The reduction of elimination was proportional to the restoration of irritability in Ringer's solution. By that is not meant that the elimination of phosphoric acid, or the alteration in the condition of the investing layers accompanying increased permeability, is the sole cause of fatigue.

Besides the elimination of phosphoric acid that of nitrogen was likewise investigated in a few cases. With short periods the eliminated nitrogen was insufficient to enable conclusions to be drawn. With longer periods, however, an unmistakable parallelism existed with the quantitative phosphoric acid elimination. In muscular activity it is obvious that a physical process is at play, besides the chemical one of the formation of acid from lactacidogen, which depends on an alteration of the permeability of the investing layers. In muscular recovery the acid that has been formed is removed by oxidation and by reconversion to carbohydrate (lactacidogen). This process represents chemical recovery. The increased permeability induced by the exothermic process of acid formation must give way to an endothermic detumescence process on the disappearance of the acid, which latter process is to be regarded as physicochemical recovery.

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Researches on Potassium Paralysis.

*Hans Vogel, Hoppe-Seyler's Ztschr. f. physiol. Chem., 118:50,  
Berlin, Jan. 12, 1922.*

Overton maintained that potassium salts, so far as they cause reversible paralysis, do not penetrate into the interior of the muscle fibers but produce their paralyzing action by altering the condition of the investing sheath. This alteration consists in a loosening which leads to increased permeability. Increased muscular phosphoric acid secretion was assumed to be the expression of increased permeability of the investing sheath of muscle fibers. In the experiment both gastrocnemius muscles were attached to platinum electrodes and suspended in Ringer's solution (0.6% Na Cl; 0.03% KCl; 0.02% CaCl<sub>2</sub>; 0.02% Na<sub>2</sub>CO<sub>3</sub>), at a temperature of tap water, which varied between 11° and 14°. Phosphoric acid was estimated nephelometrically.

All of the experiments failed to disclose increased elaboration of phosphoric acid in potassium paralysis. On the contrary, it was found that with prolonged action of isotonic potassium sulphate solution a considerable diminution of phosphoric acid took place, as compared with control experiments in Ringer's solution. Therefore, potassium salts not only do not increase the restricted permeability of the investing sheath of muscle fibers but actually diminish the same when the action is prolonged. The rapidity with which complete muscular non-irritability sets in at a certain point on the coil, after the muscle is placed in the solution of a potassium salt, depends on the muscle's permeability as determined by the degree of phosphoric acid elimination. The higher the permeability of the intumescent layer the more rapidly paralysis sets in. This showed itself also when a muscle was placed in isotonic sucrose solution, which though not effecting complete paralysis merely diminishes contraction but increases the elimination of phosphoric acid. In this case the appearance of potassium paralysis is accelerated. Accelerated potassium paralysis is also observed when muscular work is maintained until a certain amount of fatigue manifests itself, inasmuch as considerably increased permeability in conditions of extreme fatigue facilitates the action of potassium salts. The experiments showed, further, that previous active work accelerates considerably the appearance of potassium paralysis. Of two muscles undergoing the same treatment the one eliminating more phosphoric acid is more rapidly paralyzed by potassium. If the phenomena observed in the recovery from paralysis be studied in a similar manner to its production, it is seen that a muscle rendered nonirritable by potassium at a definite coil interval by no means regains its irritability toward the same stimulus quickly when replaced in Ringer's solution, but that a long interval will elapse before irritability sets in again. The recovery of a muscle paralyzed by potassium was greatly expedited by the transient action of isotonic sucrose solution. This experimental result conforms to the conception that the use of an isotonic sucrose solution, for increasing the permeability of investing sheath of muscle fibers, facilitates the penetration of potassium into the interior of the fibers as well as its extrusion from the same. Accordingly the muscle paralyzed by potassium, when replaced directly in Ringer's solution, recovers more slowly from paralysis than does muscle rendered nonirritable in isotonic sucrose solution on replacement in

Ringer's solution. Increased permeability due to sucrose solution is added to that produced by fatigue. From the fact that, in contradistinction to potassium paralysis, the paralysis in isothonic sucrose solution disappears rapidly after replacing the muscle in Ringer's solution, it is clear that the attacking point of sucrose solution lies in the superficial muscle fibers, while that of potassium salts is situated in the deeper layers. A gastrocnemius survives longer in an isotonic solution of a noninjurious potassium salt than a control muscle placed in Ringer's solution under otherwise similar conditions. This would seem to rest on the reduction of the permeability of investing sheaths induced by prolonged potassium paralysis which manifests itself in greatly diminished elimination of phosphoric acid.

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**The Influence of Asphyxia on the Permeability of Investing Sheaths of Muscle Fibers.**

*Max Simon, Hoppe-Seyler's Ztschr. f. physiol. Chem., 118:96, Berlin, Jan. 12, 1922.*

The irritability of frogs' muscles persists for a considerable time after their removal from the organism if they are adequately supplied with oxygen, and recovery after previous muscular work takes place much more rapidly in a medium of oxygen. By placing the muscles in pure oxygen, rigor mortis may be prevented. According to Flethscher muscular recovery in oxygen is attended by increased formation of carbon dioxid, the lactic acid formed during work being simultaneously diminished, the formation or reduction of phosphoric acid accompanies this process. With increasing recovery phosphoric acid elimination is reduced. In accordance with this conception increased permeability under muscular work results from intumescence of the investing layers, which are almost impermeable while at rest, under the action of lactic and phosphoric acids formed at the moment of contraction. Fatigue results from this because the increased permeability, which sets in at the moment of contraction under influence of acid formation, becomes more and more persistent even during and after relaxation of the muscle, if stimulation is repeated with sufficient frequency. The greater the persistence of increased permeability the greater is the fatigue.

Asphyxia of the muscle seems intimately related to this fatigue. Simon investigated whether asphyxia-like diminished irritability of the resting muscle under temporary oxygen deficiency is related, like fatigue, to a condition of increased permeability of the investing layers. The experimental method resembled that adopted by Embden, Adler and Vogel. Frogs' gastrocnemius muscles were suspended between two platinum electrodes in Ringer's solution. The Ringer's solution was tested for phosphoric acid by Pouget Chouchak's method. Asphyxia was effected by interrupting the supply of oxygen and removing the latter with hydrogen introduced from a Kipp apparatus. The condition of permeability was examined by determining phosphoric acid elimination of muscles kept under precisely comparable conditions and by a comparison of the rapidity with which potassium paralysis set in. For initiating potassium paralysis an isotonic solution of potassium chlorid was employed.

The experimental results were as follows: If a muscle supplied  
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with oxygen is subjected to anaërobic conditions by the introduction of hydrogen, increased elimination of phosphoric acid takes place frequently before any appreciable reduction of irritability becomes manifest. This is to be taken as the expression of a condition of increased permeability of the investing sheath of muscle fibers during asphyxia, and the elimination of phosphoric acid increases more and more. If the oxygen supply be restored in time the increased permeability disappears fairly rapidly and the reëstablishment of irritability proceeds parallel with the reëstablishment of normal impermeability. That potassium paralysis results in the asphyxiating muscle from the addition of the same potassium solution much more rapidly than the control muscle supplied with oxygen, was shown both by increased elimination of phosphoric acid and by the accelerated penetration of potassium ions into the muscle interior in conditions of increased permeability of the vesting layers. It is possible that apart from the increased permeability of the sheath the internal muscular apparatus is injured and rendered more sensitive by potassium paralysis under the influence of oxygen deficiency. Again, the oxygen muscle can be more rapidly irritated in Ringer's solution than the hydrogen muscle. In an equally prolonged suspension in potassium solution the hydrogen muscle takes up more potassium than the oxygen muscle, owing to the greater permeability of its investing layers. The muscular changes occurring in asphyxia and fatigue are, therefore, extraordinarily similar. In both cases it is probable that the formation of acid in the interior of the muscle fibers produces increased permeability of the investing layers as well as diminished irritability.

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**The Influence of Chemical Composition and Physicochemical Structure on the Function of Frogs' Muscles.**

*Hans Behrendt, Hoppe-Seyler's Ztschr. f. physiol. Chem., 118:121, Berlin, Jan. 12, 1922.*

The rapidly acting and easily fatigued white musculature of the rabbit contains a much larger amount of lactacidogenic phosphoric acid, and much less residual phosphoric acid, than the slow but permanently functioning red musculature. In the frog, also, decided differences in the functional behavior of two adductors—gracilis and semimembranosus—on the one hand, and the gastrocnemius on the other, have been observed. These adductors contract more rapidly and work with greater efficiency than the gastrocnemius muscles, but are more easily fatigued. From this it was concluded that more energy material is at the disposal of the gastrocnemius than of the adductors and that muscle fatigue is the expression of the consumption of chemical substances. Quantitative chemical methods should, therefore, throw light on this question. The adductor muscles should be characterized by a larger content of lactacidogenic phosphoric acid and less residual phosphoric acid than the gastrocnemius. In the chemical experiments the gastrocnemius and the semimembranosus were employed. The distribution of phosphoric acid was determined in both these muscles. Lactacidogenic phosphoric acid and residual phosphoric acid were estimated by Wechselmann and Adler's method. Glycogen was estimated by Plügeri's short method. For the determination of glucose Ma-

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quenne's method was chosen. The comparative chemical investigations show that during the autumnal months the glycogen content was quite uniform; where differences occurred the gastrocnemius always contained more glycogen than the adductors. As regards distribution of phosphoric acid fraction the amount of inorganic phosphoric acid was nearly always greater in the adductors than in the gastrocnemius. Appreciable differences in the amount of lactacidogenic phosphoric acid in both muscles could not be determined. The proportion of residual phosphoric acid was higher in the gastrocnemius than in the adductors. At any rate, the chemical differences between gastrocnemius and adductors were too slight to furnish an explanation of the extraordinary difference in the physiologic behavior disclosed by Bürker's researches.

As fatigue, according to Embden, Adler and Vogel, is the expression of an injury to the relative impermeability of investing sheaths it is possible that thinner sheaths are more exposed to such injury than thicker ones. Therefore, it is not excluded that the three characteristic differences in the functional behavior of the adductors (more rapid contraction, greater efficiency and easier fatigue) in comparison to the gastrocnemius, can be explained by the slight thickness of the limiting sheath in question. To this end experiments were undertaken, the gastrocnemius and semimembranosus being employed. Both muscles were attached between platinum electrodes and suspended in a virtually equal quantity of Ringer's solution, through which oxygen bubbled, at 14°. Phosphoric acid was estimated in the customary manner and a few times the estimation of nitrogen elimination was estimated, in addition, by Kjeldahl's micromethod. Experiments were also conducted on potassium paralysis and the behavior of resting and fatigued muscles, as well as the behavior in sucrose and potassium paralysis. The elimination of phosphoric acid is increased more in amount and duration in the semimembranosus than in the gastrocnemius, but after a considerable time, the former no longer elaborates an appreciable amount of phosphoric acid. When both were then stimulated in the same circuit the more easily fatigued semimembranosus eliminated more phosphoric acid than the gastrocnemius and, after stimulation was ended this increased elimination persisted longer in the semimembranosus. Under all conditions the paralysis of the semimembranosus in physiologic sucrose solution set in sooner than that of the gastrocnemius, even if the latter had become extraordinarily fatigued by work. The elimination of phosphoric acid was always greater in the semimembranosus than in the gastrocnemius. Further, the behavior of both muscles in potassium paralysis was observed. Potassium paralysis set in simultaneously, or nearly so, in both muscles if the muscles were in a fresh, unstimulated condition, or if, after prolonged rest, they showed approximately equal permeability as measured by the elimination of phosphoric acid. Previous stimulation accelerated paralysis and this acceleration was greater in the semimembranosus than in the gastrocnemius. The fact that work induced a greater degree of paralysis in the semimembranosus than in the gastrocnemius proves that the alteration of the investing layers which is manifested by increased permeability under work, is in accord with the conception that the permeable investing layers, whose condition determines the rapidity of appearance of potassium paralysis, are thicker in the gastrocnemius than in the semimembranosus. As regards the disappearance of potassium paralysis in

both muscles the replacement in Ringer's solution always restored the irritability of the gastrocnemius sooner than that of the semimembranosus. When both potassium paralyzed muscles were transferred to a sucrose solution, the time required for the recovery from paralysis in the semimembranosus was always less than in the gastrocnemius. The appearance of this paralysis seemed to be accelerated by previous treatment with sucrose solution, more in the semimembranosus than in the gastrocnemius. When both muscles were subjected to anaërobic conditions by the introduction of hydrogen into Ringer's solution, greater elimination of phosphoric acid was observed in the semimembranosus than in the gastrocnemius. The acceleration of potassium paralysis that is brought about by suffocation did not, however, set in earlier in all cases in one of the two muscles. Regarding the appearance of potassium contraction it may be stated that the very protracted gastrocnemius contraction shows that muscle's superior capacity for tonus contraction. The degree of contraction after addition of potassium depends on the muscle's condition and is the larger the fresher and more rested the muscle is at the time. In the experiments on phosphoric acid and nitrogen elimination the gastrocnemius was found to elaborate, almost without exception, less nitrogen and less phosphoric acid in equal periods and under the same external conditions than the semimembranosus.

The conclusion, therefore, seems justified that the characteristic functional differences between semimembranosus and gastrocnemius are explained by the more delicate structure of the former's investing sheath and that on this depends the capacity of the semimembranosus for more frequent contractions and greater efficiency of work, but also easier fatigue.

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**The Osmotic Action of Dehydrated Frogs' Muscles and of Those Poisoned by Glycerin, and the Loss of Muscle Proteins.**

*Paul Dux and Artur Löw, Biochem. Ztschr., 125:222, Berlin, Dec. 18, 1921.*

Muscles kept in physiologic sodium chlorid solution are subject to change in weight. This was studied with the aid of muscle intumescence curves. Glycerin is a pronounced dehydrating agent and causes changes in the condition of muscles. Both substances induce very high and persistent contraction by dehydration, probably because the granules, after being subjected to the action of a dehydrating agent, are in a condition of relative detumescence and are, therefore, capable of taking up blind with great avidity. Investigations were therefore undertaken for the purpose of studying the intumescence curves in dehydrated frogs and frogs poisoned by glycerin, and of determining to what extent the accumulation of lactic acid in dehydrated muscles influences the curves. The gastrocnemius muscles were employed for the experiments. One was used as a control, while the right muscle was examined for the influence of accessory factors. After the body weight of the experimental animal had been determined, its posterior thigh was amputated by a ligature, the gastrocnemius removed, dried, and placed in a 0.6% sodium chlorid solution. The frog was then deprived of food and water for twenty-four hours. If a loss of 20% in weight resulted, the animal

was killed, the gastrocnemius was removed, dried, weighed, and placed in a 0.6% sodium chlorid solution. In addition, the intumescence curves of muscles after the beginning and at the height of glycerin-poisoning were studied.

The results and observations show that dehydration causes a steep rise and a sudden fall of the detumescence curves in osmosis; this was more marked in glycerin-poisoning than in simple dehydration. Furthermore, the loss of water in glycerin-poisoning often amounted to nearly one-fifth of the normal weight of the muscle.

The influence of lactic acid accumulation, in addition to dehydration, was also investigated, and increased production of lactic acid studied in its rôle as the cause of the alteration of the intumescence curve. The estimation of lactic acid was made by Meyerhofer's method. The weighed frog's muscle was triturated with 90% alcohol, filtered after twelve hours, concentrated, and digested with ammonium sulphate solution. The filtrate was acidified with 50% sulphuric acid, shaken with sodium carbonate solution and amyl alcohol, concentrated and, after evaporation of the amyl alcohol, the lactic acid was converted into aldehyd with four-hundredth-normal potassium permanganate solution and distilled. Titration followed with fiftieth-normal iodin solution. The experiments showed clearly that in dehydrated muscles an accumulation of lactic acid takes place and that is able, ultimately, to promote coagulation of the albuminoids in the muscle.

As regards the physiologic interpretation of the descending intumescence curves, this, as well as the relaxation of contracture in rigor, does not seem to depend solely upon processes of disintegration due to lactic acid accumulation, but also, at the same time, upon true coagulation (processes of dehydration, deionization, detumescence). Weber's statements as to the passage of albuminous substance from the muscle into the surrounding liquid in experimental intumescence were confirmed. On the other hand, his contention that lactic acid always promotes intumescence but never promotes coagulation was shown to be erroneous, inasmuch as muscle proteins are precipitated from ammonium chlorid muscle-plasma even by small amounts of lactic acid. The proof of the high degree of dehydration and the characteristic osmotic behavior of glycerinated muscles seem to lend support to Fürth's muscle contraction hypothesis. Fürth believed that the intumescence water for the fibrils is derived not from outside, from the sarcoplasm, but that the displacement of water is effected within the doubly refracting parts of the muscular fibrils, in such a manner that ultramicroscopic elements become intumescent at the expense of the surrounding albuminous liquid.

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**Muscle Tonus. I. The Path of Tonic Innervation from Central Nervous System to Muscle.**

*E. A. Spiegel, Pflüger's Arch. f. d. ges. Physiol., 193:7, Berlin, Dec. 8, 1921.*

According to Frank's theory, the skeletal muscles receive impulses through the posterior spinal roots, and the loss of tonus following section of these roots is therefore due not only to the destruction of the afferent portion of the reflex arc but also to the loss of centrifugal stimuli.

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lation. In order to prove this view, studies were made as to the effect of section of both posterior spinal roots in the region of the lumbosacral spine (in frogs) upon muscles the tonus of which had previously been altered by unilateral extirpation of the labyrinth. If one defines muscle tonus as a state of tension causing a definite activity of the skeletal portion into which the muscle is inserted, and continuing as long as this bony part remains immobile, one may well speak of a labyrinthine effect. These labyrinthine changes are in no way affected by sectioning the posterior roots. The tonic innervation of muscles is therefore not effected by way of fibers passing through the posterior roots (contrary to Frank's view), but rather along the same fibers which effect contraction during motion. The central mechanism of locomotion, as well as the activity of the skeletal muscles, concern the anterior cornual cells.

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Determination of the Current Density and the Relation of the Density to the Excitation Process.

*W. Steinhausen, Pflüger's Arch. f.d. ges. Physiol. 193:171, Berlin, Dec. 24, 1921.*

Although the physiologic current actions essentially depend, as is known upon the current density, only a limited number of direct measurements and experiments for the determination of this density exist. The threshold current density can be determined by dividing the intensities of the threshold current by the smallest transverse section of the stimulated muscle in which the muscular fibers are still present. For the sartorius muscle of the frog, Steinhausen obtained as threshold current intensity  $1' (to 6) \times 2 \times 10^6$  amperes; by measuring the serial cross-sections, the threshold current densities were found to be, on an average,  $3 \times 5 \times 10^6$  amperes per square millimeter. Upon comparison of the values obtained for different muscles, a satisfactory agreement is found, in view of the many sources of error. Of all the tissues, the nerves are best adapted for the study of this question; for this, it is sufficient to determine the stimulation threshold of the intensity of the simple longitudinal current, and the nerve cross section. From this the much smaller value—as compared with the muscle—of  $1 \times 14 \times 10^6$  amperes per square millimeter results.

The distribution of the current is in only a few cases simple enough to be experimentally demonstrable. One such case is the current distribution in a muscle with parallel fibers, when flat electrodes are used, whereby the current density in each transverse section is inversely proportional to its surface area. The muscle represents itself as a blunted cone, after it is pointed at the ends. Mathematical conclusions demonstrate that the number of stimulated fibers is a linear function of the stimulation current intensity; experimental results support this finding. The irritation stimulation thresholds are in exact inverse proportion to the transverse sections at the extreme muscle ends. The relations between density of current and number of stimulated muscle fibers may, according to certain assumptions, be computed but not proved by experiment, since, in the summated reaction of the muscles, numerous new changes come into play. If the increase in stimulation depended alone upon an increase in the number of fibers, the maximum stimulation would be reached when the current density had exceeded—even

in the largest muscle cross-section—the given threshold current density. Moreover, curves, the ordinates of which represent the height of contraction, and the abscissae of which represent the current intensities, and which are applied for the ascending and descending direction of the current, intersect each other at about 3.5 times the threshold current intensity—i.e., there is an inversion of the relation of the contraction heights in the case of strong currents. The primary cathodal permanent contraction plays a dominant rôle. In the case of nerves one can ascertain current density and direction of the current waves without difficulty, but not, however, the value of the individual current directions in relation to their physiologic stimulative power, because too little is known regarding the influence of the angle between the course of fibers and the direction of the current.

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**Studies of Cerebral Function in Learning. IV. Vicarious Function after Destruction of the Visual Areas.**

*K. S. Lashley, Am. J. Physiol., 59:44, Feb. 1, 1922.*

The normal visual area of the cerebrum was destroyed in 14 rats. The animals were then trained to discriminate differences of light intensity. When the habit was acquired a second operation destroyed some other cerebral area and tests were made to determine the loss or retention of the habit after this operation. The habit survived the destruction of any given third of the cortex left intact by the first operation. Only a small area in contact with the floor of the cranial cavity remained unexplored; it seems certain that there is no cerebral localization in vicarious functioning for the visual area. Lashley suggests 3 explanations of the above results: (1) the visual function may have been assumed by the areas remaining unexplored by the second operation; (2) the habit may have been learned wholly at subcortical levels; (3) a diffuse functioning of the cortex may have obtained, such that the various parts were equipotential in the habit. The destruction of the entire cortex seems to result in the loss of habits acquired by vicarious functioning and to limit the possibility of forming complex visual habits. The explorations were extensive enough to make it improbable that any localized area functioning in vision remained intact in all the animals. No other possibility remains, save that the area functioning vicariously overlapped the different operative fields so that enough of it survived each operation to retain the visual function. But the variations in the operations performed make it certain that no limited area could have remained in part undestroyed in all the operations. The conclusion is, therefore, that in vicarious functioning all parts of the cerebral cortex (with undetermined limits of size) remaining intact can mediate the habit.

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**The Chemistry of Phosphorus in Brain Activity.**

*William Henry Porter, Med. Rec., 101:402, Mar. 11, 1922.*

Phosphorus, like other inorganic elements acts by virtue of its irritating and, in this sense, poisonous properties. Phosphorus when pure is highly toxic, but when combined with sodium or calcium and mag-

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nesium it loses almost all of its poisonous properties and becomes one of the essential constituents of the animal economy. A second manner in which phosphorus reaches the fluids and tissues of the body is when it is combined with carbon, hydrogen, nitrogen and oxygen to form lecithin, nucle-albumin, nucleic acid, phytin. Bunge shows how these complex phosphorus-bearing bodies are produced and how they enter the system in the various food elements. In the breaking-up of this highly complex phosphorus-bearing molecule it is reasonable to suppose that for an instant the phosphorus atom is free, and has an oxidative stimulating action upon the protoplasmic masses, thus generating an inherent central nervous impulse, which not only augments the cell activity per se in which this change occurs but is reflected in all parts of the economy by the nerve fibers springing from the cells. This being true, it is easy to accept the generally good effects which follow the use of this class of compounds physiologically and when used as therapeutic agents. The free phosphorus after serving its purpose as such, is quickly bound up again in disodic monohydrogen phosphate. The urea formed by this recombination, being freely soluble and non-irritating, is easily carried by the blood stream to the kidneys for its final elimination from the system. At this point it requires the expenditure of a large number of oxygen atoms to completely reduce these lecithin compounds, the same as occurs in reducing the proteins. This presupposes that a high degree of energy must be evolved from these chemical changes. There is also produced a relatively large amount of carbon dioxid at the same time with only a small amount of water. The carbon dioxid at once enters into combination with the carbonate of soda always present in the fluids and tissues of the body, causing it to be changed into a bicarbonate. This latter salt is the normal carrier of carbon dioxid and water from the seat of formation to the lungs. So far as is known to Porter the production of disodic monohydrogen phosphate, from these highly complex phosphate-bearing compounds is a newly revealed fact, and gives to the physiological economy an inherent source of this absolutely essential alkalinizer of the system. When using phytin or any of these other natural phosphorus-bearing compounds as a food or therapeutic agent, they will all produce this special form of phosphate. Hence they will not only enhance brain and spinal power, but will also tend to produce more perfect assimilation. When using phytin to supply the system with phosphorus, we secure molecule for molecule just twice as much phosphorus as when using lecithin. These facts sustain the truth that these complex phosphorus-bearing compounds have stimulating and energy-producing properties outside of their simple heat-producing power.

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The General Structure of the Nutritive System of the Central Nervous System in the Light of the Chlorid Method.

Franz Groebbel, *Pflüger's Arch. f. d. ges. Physiol.*, 193:128, Berlin, Dec. 24, 1921.

The staining methods which may be used in examining the central nervous system never represent, at the same time, the various morpho-  
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logicohistochemically differentiated elements, so that the relations of such elements to each other can be determined only through the combination, actual or hypothetic, of the methods. The inorganic substances within the nervous central organs were entirely neglected by the usual technic, although they are of great physiologic importance. This applies to the chlorid and phosphate of the K, Na and Ca histochemical methods, which would represent chlorid and phosphate, although ignoring the cations, while the result of the K, Ca, and Na determination would concern the elements present in forms other than salts. Possibly in many staining procedures which are usually attributed to organic substances, salts play an important part; this is probably true for the methods of Golgi, Bielschowsky and Cajal. Groebbel has placed fresh material in weak nitric acid, silver nitrate solution, treated with formol and stained according to Nissl's method. The silver solution may attack chlorids and phosphates freely present in the tissue, whereupon silver phosphate deposits also appear, together with the silver chlorid ( $\text{AgCl}$ ) originating in the light. As the second dominating material, lipoids come into consideration; various experiments render it probable that the brown color of certain tissue parts appears independently of the presence of chlorid. Thirdly, black reaction products are found on the mesodermal structures; these are not silver phosphate and their histochemical nature is still unexplained, but they are probably dependent upon the connective elastic tissue.

In the silver preparation, the medullary substance is dark and brownish and the gray substance becomes a brighter yellow, because the ganglion-cells remain uncolored, while in areas where gliose tissue predominates, a darker color appears. The silver nitrate protein compounds appearing under the influence of the silver nitrate hold the silver chlorid fast, after precipitation, where they were before treatment. All those structures affected by the Nissl principle or the polychrome methylene-blue, do not take the stain. The method, therefore, represents nervous, gliose and mesodermal tissue simultaneously, gives histologic expression to the chlorid phosphate distribution, and reveals not only solid substances but also fissures. The Nissl substance is the nutritive material of the cells, the arrangement of which, under certain circumstances, may represent the course of the underlying nutritive stream. This stream flows from the arterial vascular system by way of the lymphatic capillaries to the periphery of the ganglion-cells, where there is an exchange of substance with the part to be supplied, and, at the same time, direct communication with the nutritive waste system.

This is characterized by the dendritic trophospongium, which ends in a net-like formation in the venous capillaries, then leads through the pericellular trophospongiosis glia net, which also ends in a net-like formation around the venous capillaries. The feeding of the axis cylinder is not from the cell, but probably through the surrounding glia, in which an afferent and an efferent nutritive system are established. Therefore the glia net around the cells of the spinal ganglia and in Schwann's sheath of the peripheral nerves is to be considered as a pericellular, trophospongiosis apparatus. Illustrative microphotographs and schematic diagrams furnish further details.

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**The Nutritive Reaction of the Dendrites and Its Relation to General Neurobiotaxis.**

C. U. Ariëns Kappers, *Encéphale*, 17:1, Paris, Jan., 1922.

The functions of the dendrites and perikaryon are both trophic and conductive. It is important to determine the relation between these two very different functions. The embryonal development of the dendrites clearly shows their connection with nutrition, which implies that they are probably concerned with the assimilation of oxygen. The nutritive influence is indicated by the situation of the dendrites toward the cortical periphery. In a preparation made from the frog, Kappers has noted actual protrusion of the dendrites beyond the surface of the convolution. The marginal situation of the dendritic plexuses may be specially well studied in fishes. The cortical surface is closely related to nutrition. This opinion is confirmed by modern studies on oxygen and oxydases. Ehrlich has sought out reducing centers, Unna has endeavored to find oxidizing areas. He has proved that the Nissl bodies contain much oxygen. Such oxygen reservoirs are acid. The dendrites and perikaryon also contain oxygen. Labile oxydases (oxydons) occur in all parts of the nerve cell except the axon. In fishes, the author finds oxdases present in the dendrites and perikaryon, absent in the nucleus and axon. The dendrites and perikaryon grow in the direction of the stimulus, probably through the influence of electrical changes. Growth of the axons is anodal, that of the dendrites cathodal. Electrical conditions in the axon cause the formation of layer of cations in the internal periphery. These ions may be potassium. The external surface is negative. The electrical conditions favor nutrition. The growth of the cell toward sources of nutrition may coincide with its growth toward sources of stimuli. The two influences thus act together and reinforce each other. The theories of Child do not differ greatly from the conception of Kappers himself, who, however, has never stated that the electric current directing the growth of neurons originates only from other neurons. It is self-evident that such currents may be derived from many sources (skin, muscles, glands). Kappers does not agree with Child that axons develop in a plasmodesma. Furthermore, he has not neglected neuronal metabolism, as shown by his remarks on the influence of the tigroid substance on tropism. Child has misinterpreted Kappers' conception of the division of electrolytes. Sensory nerves terminate in expansions which are not sharp-pointed, but ring-shaped. This condition suggests that the surface receiving the stimulus may possibly behave like an electrical condenser. The motor terminations are more or less sharp-pointed. Axons may penetrate into the perikaryon; the dendrites never do so. In other words, motor terminations may enter sensory protoplasm, but sensory protoplasm does not enter that of the axon. The significance of this condition is not yet fully explained. Research indicates more and more that electrical conditions constitute the most important influence in the development of the neurons, both with respect to their mutual relations and with their relations to peripheral structures. However, other forces must be borne in mind. Neurobiotaxis includes all the factors of the life of the neuron.

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**The Pathway for Visceral Afferent Impulses within the Spinal Cord.**

*Loyal E. Davis, Am. J. Physiol., 59:381, Feb. 1, 1922.*

This series of investigations to determine the normal response from stimulation of the thoracic sympathetic nerve was conducted upon full grown cats which were given urethan by intraperitoneal injection. After isolating the sciatic and brachial nerves on one side, the carotid artery was prepared for a blood pressure tracing. A tracheal cannula was then inserted and connected with an automatic compressed air machine which gave an interrupted supply of air at intervals corresponding to the normal respiratory rate. The pressure under which the air entered the lungs did not exceed 2 mm. Hg. In all animals both vagus nerves were divided in the neck. Following this procedure and after mass ligation of the vessels in the chest wall, the thorax was opened on one side parallel to the course of the seventh rib. The thoracic sympathetic nerve was then isolated just before it pierced the diaphragm, ligated and divided distally. It was then carefully freed from the surrounding tissue and the rami communicantes of the tenth dorsal to the thirteenth dorsal segments inclusive were divided. A heart lever was then attached to the diaphragm for the direct recording of its movements. Stimulations were effected through an inductorium and electrode giving a tetanizing current. The animal's legs were securely tied to the board to prevent such movements as would influence blood pressure. In addition to the carotid and respiratory tracings, the pupils, corneal reflexes and movements of struggling were also observed.

In another series of animals, various spinal cord lesions were produced at the level of the second dorsal segment, under strict surgical asepsis. The lesions consisted of dorsal hemisections, complete lateral hemisections, sections of the lateral funiculi, leaving the posterior gray columns intact, anterior hemisections and complete transverse section of the spinal cord. After death, the level of the lesion was determined accurately at autopsy and a portion of the cord including the lesion was removed and stained by the pyridinsilver method of Ranson. Serial sections were subsequently made and microscopic verification of the lesion was sought. The experiments were first made upon normal cats and then upon cats which had been subjected to the various lesions of the cord. Study of the graphic results shows that dorsal hemisection of the cord, which destroyed both posterior funiculi and posterior gray columns, had no effect upon the pressor responses obtained from the thoracic sympathetic nerve. This type of lesion very definitely prevented a pressor response from stimulation of the sciatic nerve. This fact alone eliminates the posterior funiculi and any part of the posterior gray columns as the pathway for the conduction of this type of visceral afferent impulses. Complete lateral hemisection does not cause a disappearance of the pressor response to thoracic sympathetic stimulation. This is true whether the nerve on the side of the lesion or on the opposite side is stimulated. This strongly suggests that whatever the pathway within the cord, it obviously must be one which ascends partly on the homolateral and partly on the contralateral side. Section of the lateral funiculi and including a portion of one of the anterior gray columns has resulted in a slight decrease in the height of the pressor response, but the characteristic rise still remains. It is evident that the

pathway is not a long crossed tract situated within the lateral funiculi nor can the pathway be located in the anterior funculus, since a lesion destroying these latter funiculi does not influence the blood pressure curve. The only lesion produced which has destroyed this pressor response from stimulation of the thoracic sympathetic nerve has been a complete transverse section of the spinal cord. It is reasonable to presume, therefore, that the impulses arising from the viscera, transmitted through the thoracic sympathetic nerve and giving rise to vasomotor and respiratory responses, are conducted upward by relays of short spinal paths with synapses in the gray matter of the spinal cord. Since complete transection of the spinal cord at the level of the second thoracic segment eliminates the pressor response, it is obvious that the reflex arc is not complete within the spinal cord and that the visceral afferent impulses must reach the bulbar vasomotor center before they can become effective in producing a pressor response.

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**Chemical Processes in Antagonistic Nerve Action.**

*Leon Asher, Pflüger's Arch. f. d. ges. Physiol., 193:84, Berlin, Dec. 8, 1921.*

Based upon the communications of Loewi concerning the humoral transference of cardiac nerve action Asher observes that he used the hypothesis of different chemical processes in his investigations on antagonistic nerve action. Experimental work by P. Panowa in 1918 and 1919, not yet published, upon frogs' hearts, revealed the following: If a heart is kept in a potassium-free Ringer's solution, the heart beat becomes gradually weaker. If such heart is brought to complete vagus paralysis, and then, after removal of its contents, the vagus is stimulated and another heart, similarly altered, is placed in the solution, there occurs a marked improvement in the beat of this second heart, or a restoration of pulsation if the latter has stopped. Obviously the stimulation of the vagus induced certain alterations within the potassium-free Ringer's solution which enabled the latter to improve the precarious condition of the second potassium-starved heart.

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**Position and Activities of the Diaphragm as Affected by Changes of Posture.**

*Roy D. Adams and Henry C. Pillsbury, Arch Int. Med., 29:245, Feb. 15, 1922.*

This study emphasizes observations of the diaphragm with the subject in the lateral prone positions, which do not seem to have been given, in the literature, their proportional importance. An effort was made to select a subject as nearly as possible the average normal. Variations in different subjects, with respect to the points considered, will be of degree rather than of kind, and so a given error will not be serious. Photographs of x-ray plates show the diaphragm highest in the prone position, intermediate in the standing, lowest in the sitting. Its excursion in these positions is equal on the 2 sides. With the subject prone on the right side, the right dome of the diaphragm is higher than the left and its excursion is in excess of the proportion of 2:1. Reversal of position reverses the height and excursion of the 2 sides.

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The position of the heart, accompany the changes in position of the diaphragm, shows a wide range, its extreme excursion being 6 cm. Marginal sounds are heard over the healthy lung—over a broad area on the dependent side of the lung in lateral prone positions, because of the greater extent of the complementary space; they are heard best during vigorous inspiration following forceful expiration. The dependent lung is relatively relaxed; its diaphragmatic ventilation is in excess of that of the upper lung in these positions. Breath, voice and whisper sounds and tactile fremitus are all increased in the dependent lung (Bushnell).

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**The Significance of Respiratory Chest Expansion.**

*Scheidt, Deutsch. med. Wochenschr., 48:189, Berlin, Feb. 9, 1922.*

The mechanical conditions for the respiratory function of the thorax, as far as they can be ascertained by the anthropometric method at all, can be best determined by: (1) the absolute proportion between the height of the body and the circumference of the chest; (2) the quotient of expansion ( $\frac{\text{circumference of the chest in expiration} \times 100}{\text{circumference of the chest in inspiration}}$ ) or by the absolute difference between the circumferences of the chest during quiet breathing at the lowest point of inspiration and at the highest point of forced expiration; (3) the thoracic index.

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**The Reflex Produced by Chemical Stimulation of the Deeper Respiratory Passages.**

*E. Horne Craigie, Am. J. Physiol., 59:346, Feb. 1, 1922.*

The main purpose of this investigation was to determine whether or not the afferent paths concerned in these reflexes from the trachea, bronchi and lungs run through the vagus nerves, and whether the primary response of the respiratory mechanism is in the direction of inspiration or in that of expiration. All the authors experiments were carried out on dogs to which had been administered morphin, chloroform and urethan. A cannula was inserted so as to lead into the lower part of the trachea and was connected with a Y-tube, of which one arm led to a recording tambour while the other was left open to allow respiration. A tube let into the side of the cannula provided for the application of the gas, which was accomplished by bubbling air under gentle pressure through a bottle of liquid ammonia or ether and then leading it through this tube into the cannula. The air was allowed to pass for five seconds. The blood pressure was recorded by connecting the carotid artery with a mercury manometer provided with a writer. From a study of the graphic results, one learns that the respiratory reflex obtained in dogs by stimulation of the deeper respiratory passages with ammonia and with ether consists of an increased expiratory effort and an inhibition of inspiration, these 2 elements appearing in varying proportions. Both the respiratory and the circulatory reflexes were entirely unaffected by section of both vagi. Craigie thinks it probable that the afferent impulses concerned pass through sympathetic branches to the spinal cord and up it to the medulla oblongata. The vasomotor response consisted of a rather gradual fall in blood pressure, followed at once by a somewhat slower return to normal.

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**Respiratory Metabolism in Toxic Glycemia.**

*A. Bornstein and E. Müller, Biochem. Ztschr., 126:64, Berlin, Dec. 27, 1921.*

The blood sugar is increased by parasympathetic irritants like pilocarpin, physostigmin cholin and acetylcholin as well as by sympathicus stimulation and also by the sympathetic toxin irritant adrenalin. After the application of pilocarpin and also of adrenalin the glycogen disappears from organs, according to the glycogen-determinations of Horemann, which seems to indicate that the blood sugar was in both cases derived from the glycogen. By using atropin the action of the pilocarpin on the sugar metabolism can be inhibited, but not the action of the adrenalin. There are, however, also quantitative differences between pilocarpin and adrenalin glycemia, the former being less considerable, although in both the greater part of the liver glycogens are transformed into sugar. Attempts were made to clarify these differences by means of restoration experiments. The experiments were carried out on man and dog with the aid of the Zuntz-Geppert apparatus, after the individual to be tested had become accustomed to the respiration in the apparatus during preliminary experiments which lasted for several days. In all other respects, the customary conditions were observed. During the experiment, the individuals were in a lying position, body rest twelve to fifteen hours after the last food intake. Only small doses, about 1.5 mg. pilocarpin, p. kg. body weight, were administered.

The respiratory quotient rises in all experiments. The rise of the respiratory quotient, however, passed off still more rapidly than the rise of the oxygen consumption. The influence of the pilocarpin upon the oxidation of the carbohydrates begins already with doses of pilocarpin that have no distinct influence on the blood sugar. Hence, in the experiments with small doses of pilocarpin an increase in the sugar combustion is noticeable which takes place partly in the presence, partly in the absence, of a blood sugar rise. Pilocarpin not only forms sugar from glycogen and causes the entrance of this sugar into the blood, but also forms an enzyme which favors sugar combustion.

In the experiments with adrenalin it was noticed that the sugar mobilized by the adrenalin is not immediately combusted; the respiratory quotient remains unchanged in the presence of high values of the blood sugar.

It is noteworthy that the combustion of the carbohydrates diminishes in favor of the fat combustion if the blood sugar is increased. It is impossible, as the experiments show, to explain the increased sugar combustion in the adrenalin glycemia by an increase in the serum fat. Tests in diabetic patients show the same rise of the respiratory quotient as observed in normal persons, caused by an increase in the ventilation of the lungs with simultaneous diminution of the tension of the aveolar CO<sub>2</sub>. In like manner, the respiratory quotient diminishes and returns to the normal value, while the blood sugar increases. Among the toxic glycemas the pilocarpin representing the parasympathetic glycemas, and the adrenalin representing the sympathetic glycemas are different in regard to the respiratory metabolism inasmuch as the pilocarpin reacts immediately with an increased respiratory quotient, a phenomenon caused by an increased sugar combustion. In contradistinction to this effect of pilocarpin the sugar formed from glycogen by the action of adrenalin

does not cause an increased sugar combustion. According to the experiments, both the sympathicus and the parasympathicus toxin manufacture sugar from glycogen, the sugar diffusing into the blood; in the finer details of this process, however, considerable differences exist which show resemblance to the behavior of the salivary gland. Stimulation of the sympathetic nerves as well as of the parasympathetic chorda tympani result in secretion from the salivary gland, but these 2 types of saliva are so different that the sympathicus saliva can be distinguished from the chorda saliva. In a similar manner, the sympathicus sugar may be distinguished from the parasympathicus sugar.

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**Cheyne-Stokes' Respiration. Part I. Production by Adrenalin.**

*F. Roberts, J. Physiol., 56:101, London, Feb. 14, 1922.*

Roberts had previously determined that the intravenous injection of 1 c.c. of 0.02% adrenalin into rabbits and cats produces in them Cheyne-Stokes respiration. Believing that the arrest of respiration was due to asphyxia of the respiratory center owing to the vasoconstrictor effect of adrenalin, he attempted to determine whether the Cheyne-Stokes respiration is also vascular in origin. He expected to find rhythmic variation in the caliber of the cerebral vessels corresponding to the rhythmic changes in the depth of respiration. Accordingly Corin's device was used to obtain a simultaneous record of the general arterial pressure and of the pressure in the circle of Willis, before and after the administration of adrenalin. Study of the tracings shows that the Cheyne-Stokes respiration, resulting in the animals after adrenalin administration, is of 2 kinds: major waves due to rhythmic changes in the caliber of the cerebral vessels, the respiratory center being quiescent, owing to oxygen want, during closure of the vessels and active when the vessels are open; the other or minor waves are associated with small oscillations in general blood pressure.

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**Influence of Glands with Internal Secretions on the Respiratory Exchange. III. Effect of Suprarenal Insufficiency (by Removal) in Thyroidectomized Rabbits.**

*David Marine and Emil J. Baumann, Am. J. Physiol., 59:353, Feb. 1, 1922.*

In a previous communication, the authors demonstrated that by removing or crippling the suprarenal glands in rabbits striking changes in the respiratory exchange resulted. The experiments included in this paper were undertaken to obtain further data on the question whether the thyroid, as previously suggested, was an important factor in the increased heat production following suprarectomy. For this purpose the following procedures were carried out on 6 rabbits: (1) "normal" heat production records (using the Haldane apparatus) were obtained over a period of two weeks; (2) the thyroid glands were removed as completely as possible, leaving the external parathyroids with undisturbed blood supplies and the heat production measured for the next twenty-three days, when, (3) the suprarens were removed and further measurements of the respiratory exchange continued until the

animals died or were sacrificed. The tabulated results show that partial but sufficient destruction of the function of the suprarenal cortex in rabbits with intact thyroids usually leads to an increased heat production. Removal of the thyroid prevents or greatly lessens the increased heat production which usually follows partial destruction of the suprarenal cortex.

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**The Effects of Adrenal Feeding upon the Iodin Content of the Thyroid Gland.**

*E. M. Black, Marjorie Hupper and John Rogers, Am. J. Physiol., 59:222, Feb. 1, 1922.*

In order to ascertain whether any demonstrable effect upon the iodin content of the dog's thyroid could be produced by long-continued feeding of adrenal deprivatives, both thyroid glands of all animals used in other experiments were first examined, weighed and tested for iodin. In the considerable number of glands thus studied there were found only slight variations, though rarely the gland on one side might appear larger than on the other. If of the same size, the iodin content was practically the same. A considerable number of animals (used in other experiments) was next treated by extirpation of one thyroid lobe, and then from 1 to 6 months later by extirpation of the second lobe. Comparison of the iodin content showed regularly a gain of about 20% to 40% in the second or retained lobe, the maximum gain being usually reached at the end of five weeks. There was no noticeable change in the total (fresh) size or weight of the organ. In some preliminary tests the adrenal derivatives were administered hypodermically; but as toxic and fatal symptoms often resulted, the adrenal residue was later mixed in the food of the animal. The daily dosage was 0.016 gm. adrenalin with an amount of adrenal residue which contained approximately the same quantity of epinephrin as determined by Follin's colorimetric method, and 4 gm. adrenal nucleoprotein material. The dogs were given these substances in their standard diet for a period of forty-five days. The tabulated results show that a somewhat hydrolyzed aqueous extract of the entire beef adrenal gland, known as the adrenal residue, when fed by mouth, can produce in forty-five days a gain in the iodin content of the dog's thyroid gland amounting on the average to 70.4%. The adrenal nucleoprotein material obtained from the entire beef adrenal gland, when fed in large dosage, shows an average increase of 50.7% of the iodin content. An amount of crystals of adrenalin which is closely equivalent in amount to the epinephrin-like material of the adrenal residue, produces little if any gain in the iodin content of the dog's thyroid.

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**The Influence of Adrenalin on Metabolism in Isolated Skeletal Muscle.**

*E. G. Martin and R. B. Armitstead, Am. J. Physiol., 59:37, Feb. 1, 1922.*

Previous observers have demonstrated a marked increase in heat production from the subcutaneous injection of adrenalin chlorid. Be-  
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lieving that direct effects of adrenalin might be demonstrable on isolated tissue, the authors studied the influence of adrenalin upon the metabolism of isolated muscle. The method employed was a modification of that of Haas by which carbon dioxide evolution is estimated with the aid of indicators. A carefully excised sartorius muscle of frog was immersed in 4 c.c. Ringer's solution made neutral with sodium bicarbonate and containing 8 drops of 0.02% phenolsulphonephthalein solution. The moment of immersion in the Ringer's solution was noted, as was the hydrogen-ion concentration of the solution, by comparison with a set of standard buffer indicator tubes. As soon as the color of the solution had definitely changed, the exact time was noted, the muscle removed from the solution, the hydrogen-ion concentration determined, and the production of hydrogen-ions per gram of muscle substance per hour computed. Such procedure was followed in the control experiments. To determine the specific effects of adrenalin, the technic was followed as described, except that the muscles were immersed in adrenalin solution in dilutions ranging from 1:5000 to 1:500,000. The tabulated results show a marked augmentation of acid production in all strengths of adrenalin solution from 1:300,000 upward. There was a fourfold increase at 1:20,000. The experiments indicate a specific dynamic action of adrenalin on individual body cells, the augmentation being of resting or basic metabolism rather than on the metabolism of function.

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**The Effect of Adrenalin on Blood-Sugar.**

*Géza Pétényi and Heinrich Lax, Biochim. Ztschr., 125:272, Berlin, Dec. 18, 1921.*

Following subcutaneous adrenalin injection the amount of sugar in the blood rises one or two hours later, according to the amount of adrenalin injected, returns to the normal in three to six hours and sinks below the normal thereafter. This course of adrenalin glycemia was investigated in adults, infants and older children. The determination was effected by Bang's micro-method and the measurement of blood volume by the method of Ernst Weiss. The normal value was determined four hours after the last meal. The blood was taken hourly for eight hours after the subcutaneous adrenalin injection of 1 mg. in adults and 0.6 mg. in 2 children aged twelve. The adrenalin preparation employed was tonogen. During the experiment the individual received no nourishment. The experiments also showed that hypoglycemia appeared four hours after the injection and persisted about five hours. The decrease of blood sugar amounted to 27%. Further experiments related to the behavior of adrenalin glycemia in individuals suffering from tetany. It was shown that adrenalin hyperglycemia is smaller in most cases, or may be entirely absent. Hypoglycemia appeared in tetany patients even when previous hyperglycemia was absent entirely. From these observations it may be concluded that the mechanism of the adrenalin effect on carbohydrate metabolism differs from that hitherto assumed. Hyperglycemia is only a partial phenomenon of this process, because it is regularly followed by a hypoglycemic stage that can not be explained by glycogen impoverishment of the organism, and is entirely independent of hyperglycemia.

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The Influence of Muscular Exercise on Normal Cats Compared with Cats Deprived of the Greater Part of the Adrenals, with Special Reference to Body Temperature, Pulse and Respiratory Frequency.

G. N. Stewart and J. M. Rogoff, *J. Pharmacol. & Exper. Ther.*, 19:87, Feb., 1922.

Normal cats, and cats after removal of the greater portion of the adrenal tissue, or removal of one adrenal and interference with the epinephrin output of the other by resection of its nerves, were subjected to prolonged and repeated spells of muscular exercise. No difference which could be attributed to interference with the adrenals was made out in the behavior of the animals as regards resistance to, or recovery from, fatigue, or as regards the changes in rectal temperature, pulse or respiratory rate. After severe muscular exertion a definite, although not a very great, depletion of the epinephrin store of an adrenal with its innervation intact, as compared with its previously denervated fellow, may be observed. But even after considerable exertion falling short of great fatigue, no depletion may be present.

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Autoplastic Transplantation of the Thymus into the Spleen of Rabbits.

S. Yamanoi, *Frankfurt. Ztschr. f. Path.*, 26:356, No. 2, Wiesbaden, 1921.

After dissecting off and partially cutting through the sternocleidomastoid between the trachea and the inner surface of the sternum, the thymus was exposed and pulled out; a piece was then cut off (hemostatic measures being taken), and transplanted into the spleen, pulled out of the abdominal cavity. In a first series of experiments, small pieces of thymus were inserted into a puncture of the spleen in the groove of a hollow sound, but as this led to the formation of pronounced capsular grooves, a special hollow needle was employed in a second series of experiments. But as the transplant, as well as the matrix of transplantation, was injured too much in the course of these manipulations, in a third series of experiments, the piece of thymus was cut off as rapidly as possible in a gentle manner, without exerting any force, and inserted in a small puncture of the spleen, which was then closed by a catgut suture. Older animals got over the operation satisfactorily, but younger animals suffered severely, some of them dying soon afterwards. With respect to 16 (out of 30) animals which survived the operation more than fourteen days, the transplant was demonstrated in 8 cases. In the first and second series of experiments, the transplant was visible in most cases only in the shape of small cellular accumulations, whereas, in the third series, the transplanted pieces exhibited a lobate structure in 3 cases. The development of the histologic aspect shows that the transplanted thymus tissue remains viable in the spleen. At first, it is true that degenerative decomposition sets in; but after fourteen days, it is embodied and healed. Regenerative processes take place in the remnant of the thymus as well as in the transplant. No myeloid areas were observed, the liver being also free from them. The aspect of the

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regeneration of the thymus transplant corresponds to that of young functioning thymus tissue. This fact tends to corroborate Stöhr's opinion; the small thymus cells occupy a special position, although it is hardly possible to discover morphologic differences between them and the lymphocytes. The latter are probably a genuine derivative of the thymus epithelia. Yamanoi did not succeed in solving, by his experiments, the problem of the eosinophilic cells in the thymus.

He arrives at the following conclusions: Autoplastic transplantation of thymus tissue into the spleen of rabbits is perfectly feasible. The success of the experiment depends on careful and rapid manipulation, the thymus tissue being very susceptible to external influences. In autoplastic transplantation, the regeneration of the transplant may reach the state of the functioning thymus and may remain viable for more than five months. Myeloid metaplasia, which is so pronounced after transplantation of bone marrow into the spleen, is never observed after transplantation of thymus tissue. The small cells of the cortex of the thymus are probably to be interpreted as a genuine derivative of the thymus epithelia. Mechanical lesions of the thymus, such as repeated partial excision, may produce an excessive regeneration or hyperplasia of the thymus; in this case, the aspect of the thymus is similar to that observed in the status thymicolymphaticus.

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**The Reticular Material as an Indicator of Physiologic Reversal in Secretory Polarity in the Thyroid Cells of the Guinea-Pig.**

*E. V. Cowdry, Am. J. Anat., 30:25, Jan. 15, 1922.*

By the application of Da Fano's modification of Cajal's silver-impregnation method to the thyroid glands of guinea-pigs, one may observe that the reticular material is not always restricted to the zone of cytoplasm between the nucleus and the follicular cavity. Reversal may take place in single isolated cells, or the reticular material may be found to be unusually close to the lumen. Apparently then, in the thyroid gland there is variability in the position of the reticular material. By means of a special staining procedure Bensley has revealed in the thyroid the true secretion antecedents in the form of tiny vacuoles which contain a dilute solution similar in its properties to the colloid of the follicular lumen, but less concentrated. Since the droplets always occur in the outer poles of the cells, Bensley concludes that the secretion is destined to direct transport into the vascular channels, and that the thyroid cell presents a true reversal of polarity in accord with its endocrine function. Hence we have in the thyroid gland evidence of physiological reversal in the direction of secretion. Since the position of the reticular material, like that of the centrosome, is a clue to the polarity of the cell, preparations made by Da Fano's method will indicate the functional polarity, or, in other words, the direction in which secretion is taking place at the moment the preparations are made. The relatively small percentage of reversals in the position of the reticular material in the guinea-pigs examined by the author, suggests to him that the balance in production of secretion is in favor of storage rather than of immediate discharge.

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**Experiments with Thyroid and Testicular Substance in Fowls.**

*Ch. Ouy-Vernazobres, Rev. fran<sup>c</sup>. de gyn<sup>c</sup>. et d'obst., 16:645, Paris, Dec., 1921.*

Recent experiments are discussed. The author worked with chicks, which had been fed powdered thyroid and testicular substance. The chicks were too small to permit of hypodermic injection. The experiments are tabulated. The sex of young chicks cannot be positively determined before the fiftieth day. The secondary sexual characters vary considerably in the different breeds. Enormous doses of thyroid and testicular substance were tolerated when given by way of the digestive tract. The chicks remained in good health. Thyroid seems to hasten the development of the plumage. Testicular extract stimulates production of the crest, in hens as well as in cocks. The redness of the erectile organs in the females was increased. The experiments should be repeated hypodermically, since much of the substance fed must be lost through digestion. The size of the male sexual organ was not increased by the substances fed. Possibly organic extracts stimulate the organism as a whole. There are many hormones. Every cause affecting an endocrine gland reacts upon the entire organism. Pezard's explanation of evolution, on the basis of harmones, is hazardous. Hormones constitute one of many ways of initiating complex reactions, but as yet nothing is really known of the reproductive impulse. Internal structure depends upon heredity, and its production remains a mystery.

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**Individual Organic Products and Their Specific Action. VI.**

*Emil Abderhalden and Ernst Gellhorn, Pflüger's Arch. f. d. ges. Physiol., 193:47, Berlin, Dec. 8, 1921.*

Endocrine organs were subjected in part to long digestion with ferment, and in part to hydrolysis with 10% sulphuric acid. Tests were then made as to the physiologic action of the end-products so obtained, on strips of cardiac muscle, on the isolated frog heart, on the esophagus and the frog's foot-web. The experiments were made on the assumption that the automatic regulation of capillary circulation is brought about chemically by internal secretions; substances obtained from the thyroid, hypophysis, thymus and other organs of internal secretion antagonize the action of adrenalin on the capillaries. Perhaps some abnormality of the organs of internal secretion will be found to explain the collapse of the finer capillary mechanism. There were some differences between the "optones" obtained through ferment action and those produced by hydrolysis. Thus, for instance, the testicular "optone" obtained by hydrolysis was able to restore the automatic function of nonpulsating strips of cardiac muscle, whereas a similar product obtained by ferment digestion could not accomplish this result, except after hydrolysis with acid. Placental "optone" obtained by ferment digestion caused an increase in contraction of the heart after a transitory diminution of the pulse; the same product obtained by hydrolysis gave negative results. Hydrolyzed products of thyroid gland and goiter stimulated the automatism and the tonicity of the surviving frog's esophagus; placental substance obtained by both methods

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caused paralysis, the acid hydrolytic product causing greater contractions in weak solutions. It appears very probable that the endocrines play an important rôle as regulators of the capillary mechanism.

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## 1b. BIOLOGIC AND ORGANIC CHEMISTRY

(1b—85)

(1b—85)

### A Micro-Extraction Apparatus.

*Fritz Laquer, Hoppe-Seyler's Ztschr. f. physiol. Chem., 118:215, Berlin, Jan. 25, 1922.*

Instead of the ether extraction apparatus, according to Lind, an extraction apparatus for quantitative determination of 2-10 mg. lactic acid is suitable. It is constructed on the Schacherl principle whereby the ether fumes stream into the extraction receiver through the same tube in which the ether, together with the substance to be extracted, flows back into the boiler piston. The glass edges at the boiler pistons and at the opening of the cooler are covered with mercury. The apparatus should give good service for micro-analysis. As the ether, condensed in the cooler and flowing out into the tube, comes out in the deepest part of the extraction receiver in large drops, the outgoing ether may, therefore, in its course be well saturated with the substance to be extracted. The extraction container holds about 7 c.c. liquid.

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### Nephelometry. A Nephelometer with a Constant Standard.

*A. Weinberg, Biochem. Ztschr., 125:292, Berlin, Dec. 18, 1921.*

In addition to other methods of analysis nephelometry has found extensive application within recent years. In this method the degree of clouding is used to measure the quantity of the substance causing cloudiness. The nephelometer-colorimeters of Kober and Kleinmann possess several disadvantages which the construction of the present nephelometer aims to obviate. Such an instrument must satisfy the following requirements. (1) The apparatus must give an intense light. (2) It must be as dust-free as possible. (3) It must permit of quick determinations and easy handling. (4) It must be placed on a firm foundation in front of the source of light. (5) The source of light must emit practically parallel rays, and equable light and must illuminate the apparatus strongly on both sides. (6) There must be no null light. (7) The apparatus must allow convenient determinations when placed vertically. (8) The eyepiece must support the orbit and be provided with a very fine opening in order to obviate equal brightness of the visual fields due to eye movements. (9) The dipping tubes, as in Kober's apparatus, must be black, with transparent soldered or cast-on ends of optically pure glass. (10) The test tubes must also be the same as directed by Kober, of transparent optically pure glass with a soldered or cast-on flat black base. (11) The whole column of fluid between the base of the dipping tube must not receive direct illumination. (12) The nephelometer must be transformable in a simpler manner into a colorimeter. On the basis of these requirements a nephelometer modeled essentially on Kober's with a fixed standard has been

constructed as follows: The dipping tube farthest from the observer is replaced by a cylindric tube which is screwed on to the apparatus. Both Nicol prisms are fixed in this tube, the lower one being adjustable against the upper one. Below the lower prism there is a space in the cylinder for the reception of a colored glass. For colorless suspensions a piece of blue so-called daylight glass indicates exactly the same color as the liquid to be examined. Beneath the prisms a detachable gypsum mirror is attached to the tripod. The inclination of this mirror permits the maximum reflection of the light emitted by the source of light upward into the apparatus. The tube containing the prisms as well as the entire internal surface of the instrument is lacquered dull black. From the experimental tables it is seen that: (1) The new apparatus has a constant zero point. (2) The parallel determinations in each experiment differ  $\pm 1\%$ , the end-results less than 0.5%, from the average. (3) The heights of the illuminated liquid columns are inversely proportional to the concentration of the suspended particles ( $x-8y$ ) with an experimental error of  $\pm 0.5\%$ . (4) The nephelometer permits comparative determinations with suspensions diluted up to one-fourth, but the accuracy is then slightly less. (5) Five parallel determinations suffice for accurate results. The accuracy of the apparatus is as high as that of the best nephelometers and in addition it is suitable for examinations of the physicochemical properties of colloidal matter. For practical clinical purposes it is advisable to test each position of the prisms with a solution of chemically pure glycogen so that the clouding produced by an unremovable substance may be expressed in values of a known glycogen solution. For substances which may be easily prepared in a pure state a standard solution of the respective substance is made. Only suspensions in which, under the same external conditions, the customary composition of the liquid to be examined has no influence on the nephelometric readings of the standard solution, and whose suspended particles do not precipitate appreciably during the determination (twenty minutes), are suitable for nephelometric investigations. With the employment of a fixed standard a quantity of only 10 c.c. suffices for a series of nephelometric determinations. As a light source the authors suggest an approximately punctiform light in the focus of a lens system in order to obtain practically parallel rays. For cleaning the nephelometer tubes a mixture of a Rochelle salt solution 5% and a sodium carbonate solution 0.5 is recommended.

(1b-87)

The Influence of Treatment with Alkali or Bromin on the Physiologic Activity and the Foaming Ability of Saponin Substances.

Ernst Sieburg and F. Bachmann, *Biochem. Ztschr.*, 126:130, Berlin, Dec. 27, 1921.

Saponins digested with cholesterin in heat entirely lose their biologic activity. Therefore, red blood-corpuscles or other cells, or even the individual as a whole, will be protected from the attack of the saponins, if cholesterin suspensions exert their influence simultaneously with the attack, or shortly afterward, or in advance. For this antitoxic process no physical absorptions are concerned, but the formation of well-characterized chemical compounds. Such saponin cholesterin al-

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ways contain the 2 components in molecular proportions. The saponin cholesterolins are only slightly soluble in water, and have no foaming ability. Complex combinations are rather loose, however, since after a long contact with an alcoholic liquid, or with ether, they dissociate into their components again. After long contact with alkali (barium hydrate), or treatment with elementary bromin, the saponin substances lose their biologic activity as far as it is expressed in hemolytic capacity. The chemical changes are unknown. The water-soluble bromin saponins lack hemolytic qualities, but maintain the foaming ability. Experiments were performed in order to ascertain whether or not, after treatment with barium hydrate or bromin, a decrease of the biologic activity of the saponins occurs, and whether the foaming ability changes, and if so, to what extent.

Examples chosen were the strongly active cyclamin and digitonin, the medium strong Merk's guaia saponin, and the slightly active quillaia saponin. The treatment with barium hydrate was carried out as follows: The saponin substances were dissolved in a 5% water solution, and the cyclamin, on account of its small water-solubility, in methyl alcohol. To this solution was added an equal volume of fifth-normal barium hydrate, and then it was kept for a time in a boiling water bath. The barium was precipitated in the hot liquid by means of an equal amount of sulphuric acid. For treating the bromin, saturated methyl alcoholic saponin solutions were used, to which was added, after cooling on ice, a 2% methylalcoholic bromin solution until the blue of the potassium iodid starch paper revealed a remaining surplus of elementary bromin. It was then precipitated with ether.

In the case of glucosids, which belong to the digitalis group from a pharmacologic point of view, and the agglucones of which, as oxy-lactones, exhibit a certain affinity for several agglucones of the saponins having the same chemical character, analogous conditions seem to prevail. In the case of agglucones of certain digitalis glucosids, the lactone ring broken by alkali at boiling heat will be changed again into lactone of the same empirical synthesis by acid; but these isosubstances are physiologically inactive. The solubility of the saponins treated with barium and bromin has been entirely changed. In order to establish the differences in the foaming capacity of the natural saponin substances and of those treated with barium hydrate or bromin, the so-called foaming number was determined. The foaming numbers indicate what percentage of a foam-giving liquid has turned into foam after a certain period of shaking, and after a certain time has been allowed for settling. They vary from 9 to a maximum of 100. The experiment was performed in the following manner. A small flask, the neck of which was graduated from 100 to 0, was filled with 10 c.c. saponin solution. This was shaken for half a minute, and then the foaming number was read off directly. As standard solutions of the saponins, concentrations of 1:100 and 1:500 were prepared; for the slightly soluble saponin this was accomplished by using 2% alcohol. The foaming capacity of cyclamin was hardly influenced at all by treatment with bromin, and that of the digitonins only in concentrations of 1:5000. The foaming numbers of quillaia saponin, Merk's saponin and guaiacal saponin were consistently lower after treatment with barium.

When, from a biologic point of view, the point of attack of the saponins is in the cholesterolin substances of the cell, and the existence

of saponin cholesterins as fixed phases is secured in some cases, then one must ascertain whether saponin substances, which will be changed in regard to their physiologic activity when treated with barium or bromin, also show a changed affinity for cholesterol in the test-tube.

A 2% saponin solution was added to 70% alcohol, and to 1 c.c. of this there were added 0.25% of alcoholic cholesterol solution, and brought up to 2 c.c. with additional alcohol. Then the test was taken which, together with the smallest amount of cholesterol, barely showed a turbidity of the leaf-like coat adhering to the walls. According to the experiments, the affinity of quillaja saponin for cholesterol was not changed by the treatment. Digitonin exhibited a weakening only after bromin. In the case of cyclamin, both methods of treatment had a weakening effect. Furthermore, the biologic effect was ascertained on the ventricle of an extirpated frog heart by means of Straub's cannula, and the terminal concentrations which cause a stasis of the ventricle were determined.

One cubic centimeter of the saponin solution in Ringer's solution was placed in the heart cannulas, and ten minutes were selected as the maximum time of observation of the toxic effect of the ventricular stasis. The experiment was based upon nontoxic conditions, and the concentrations of 1:250 up to 1:2500 were tested. Finally, the typical effect of saponin on a multicellular organism, viz., the tadpole, was tested.

All these experiments demonstrated that, following treatment with bromin, a more or less severe weakening, from a biologic point of view, took place in all cases. Treating with barium also yielded slightly less active preparations, but when treated with barium hydrate or bromin the saponin substances did not become entirely inactive as they do when in contact with cholesterol. In the experiments performed to ascertain whether or not the saponins influenced by cholesterol entirely lose their activity, it was shown that the activity was absolutely suspended both in the hemolytic experiments and in extirpated frog hearts. However, these experiments have not yet cleared up the effect of the saponins in gastro-intestinal catarrh. The saponins are glucosids and, therefore, they are subject to hydrolytic cleavage. The aglucones of the totally hydrolyzed saponins are unsoluble and unresorbable. Therefore, an influence of these aglucones on the organs outside of the gastro-intestinal canal is not to be expected. However, during passage through the gastro-intestinal canal, a certain amount of saponins of one kind or the other can be absorbed without cleavage.

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**The Determination and Significance of the Hydrogen-Ion Concentration.**

*E. C. L. Miller, Virginia M. Month., 48:660, Feb., 1922.*

Platinum black has the ability to condense or absorb large quantities of hydrogen. In the determination of the pH in a given solution, using the electrical method, platinum black is deposited by reduction on a platinum electrode; this is then saturated with hydrogen gas and serves as a hydrogen electrode. Two of these electrodes plunged into acids of different pH will give a current when electrical connections are established. The pH in the solution determines the amount of elec-

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trical potential and vice versa. This is not the same as the amount of acidity determined by titration with an alkali. By the indicator method, if to a series of tubes containing 1% peptone, neutral in reaction, is added litmus, and then increasing amounts of alkali and decreasing amounts of acid, the color in the tubes will be blue at one end, red at the other and graded between. The color of the litmus is a direct index to the pH in the tubes. If the pH of each tube to be determined electrically, this supplies a set of standards by which the pH of any unknown within this range can be determined—by adding litmus to the unknown and comparing the resulting color with the standard. For the analytical chemist, the titrable acidity of a given solution is important, but for most biological purposes the actual pH is the important thing.

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**The Determination of Hydrogen Ion Concentration.**

*Frank H. McCrudden, Pub. Health Rep. (U. S. P. H. S.), 37:334, Feb. 17, 1922.*

A normal solution of an acid is one containing 1 gm. hydrogen per liter replaceable by a base. In making up a normal solution it must be known whether the acid used is monobasic or dibasic; whether some of the hydrogen is not replaceable by a base, as is the case with most organic acids; and the whole molecular weight must be employed in figuring the number of grams to be used, not forgetting the water of crystallization of such substances as oxalic acid. A definite volume of a normal acid will neutralize the same volume of a normal alkali, but there are different properties of an acid solution than the mere neutralization of an alkali. Equal volumes of 2 acids of the same normality may have marked differences in their ability to stimulate some reaction depending upon the degree of dissociation, or the extent to which the acid breaks up in solution into its component ions. Solutions of substances which dissociate transmit electric current and are called electrolytes. The current is transmitted by the movement of the ions; the cations carry a positive charge of electricity to the cathode and are discharged, the cations being deposited as a molecule; while the negative electricity is carried to the opposite pole by the anions. Some substances in solution are not dissociated at all and are known as non-electrolytes, others are slightly dissociated and are known as weak electrolytes, while others that dissociate completely in weak solutions are termed strong electrolytes. The dissociation constant of a substance or  $K$ , is the ratio of the product of the cations and anions to the concentration of the undissolved substance or, in other words, the concentration of the cations or hydrogen ions in acid solutions is equal to the dissociation constant of the acid multiplied by the concentration of the acid and divided by the concentration of the salt. The concentration of the hydrogen ions in pure water is equal to the concentration of the hydroxyl ions and  $K$  becomes  $0.0000001$  or  $10^{-7}$ . The hydrogen ion concentration of a solution, pH, may be expressed in a number of different ways, but the simplest and the one most commonly used is the negative logarithm or 7.0 in the case of pure water, or for equal parts of acetic acid and sodium acetate 4.75 which represents  $10^{-4.75}$  or 0.000018.

It has been found that most bacteria grow best in media whose  
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pH lies between 7.2 and 7.6; typhoid, for example, preferring the lower limit, and the pneumococcus, the upper. Consequently it is important to determine the pH of a medium and adjust the reaction to the desired pH. Indicators are weak organic acids whose anion has a different color in solution from that of the undissociated acid. In acid solutions the excess of hydrogen ions diminishes the dissociation of the weakly acid indicator and the undissociated acid gives its characteristic color to the solution. In bacteriological work it is necessary to keep close to neutrality, pH—7 and fortunately there are several indicators that may be used for this region as brom cresol purple, which changes from yellow to purple between pH 7.2 and pH 6.8, and phenol-red which changes from yellow to red between pH 6.8 and pH 8.4.

To determine the pH of an unknown solution a series of 12 or more standard comparison solutions of tenths molecular anhydrous potassium phosphate and tenths molecular sodium phosphate giving a pH range from 7.8 to 8.0 must be prepared using in each 5 drops of the proper indicator. The unknown solution is diluted to a moderate extent to overcome the effect of turbidity. In the case of the standards, the turbidity tubes and the indicators are in separate solution behind each other in a comparator look. After determining the pH of the unknown by color comparison with the known standards, the unknown may be adjusted to the desired pH by titrating 5 c.c. with tenth-normal alkali until the proper pH has been obtained and then figuring the correct amount of alkali to be used to adjust the whole batch.

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**Methodical Analysis of Blood and Urine. I.**

*Ludwig Pincussen and Aristomenis Floros, Biochem. Ztschr., 125: 42, Berlin, Dec. 8, 1921.*

Because of the high price of the torsion balance, Bang's procedure of sugar estimation was modified in the following manner: a moderately deep incision is made with a Frank needle in the tip of the finger which has been cleansed of fat with ether, a large drop is allowed to form so that surface coagulation does not occur and the pipet is filled as much as possible. The pipet used must be accurately calibrated, not too narrow and absolutely clean and dry. The addition of coagulation inhibitory substances is inadvisable. The blood is aspirated into the pipet with a small syringe or with the mouth, adherent blood is wiped off and the contents are allowed to drop upon a Bang's lamina; the rest of the blood is blown on the Bang's lamina. The pipets should hold 0.1 gm. blood. The laminas prepared in this way are worked up in the usual manner.

Grape sugar in the urine can also be determined with Bang's technic: the removal of the albumin of the urine is accomplished with a 0.05% copper sulphate solution. The urine is diluted 100-fold because of the relatively high amount of sugar in diabetic urine. With the applied reagents a vacuum determination is made first of the iodin-binding substances contained in it. The difference between the hundredth-normal solution of thiosulphate used in the vacuum determination and the amount used without the vacuum divided by 2.8 gives the amount of grape sugar in the tested amount of urine. This method is very accurate, for it not only gives the amount of sugar but also of reducing substances in the urine. If it is only desired to determine the grape

sugar, a second determination of the reduction is made after the fermentation of the sugar. However, for ordinary purposes it is sufficient, if a certain medium value for the amount of grape sugar obtained in twenty-four hours is subtracted. This medium value for the other reducing substances resembling the amount of the stimulated grape sugar was found to be 2.0 gm. in a series of analyses, which must be subtracted from the daily amount of grape sugar found in the diabetic patient.

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**Methodical Analysis of Blood and Urine. II.**

*Ludwig Pincussen and Kate Momferratos-Floros, Biochem. Ztschr., 125:46, Berlin, Dec. 8, 1921.*

In the determination of acetone in the urine, because of the large quantities of material necessary with the iodometric method, an apparatus is advised which allows the use of small amounts. It consists of 2 large test-tubes each 20-25 cm. long and 2.5 cm. in diameter, of which one is used as a distilling vessel and the other as the recipient. The tubes are stoppered with well-fitting corks and a cooler is not necessary. According to whether the free acetone alone is to be determined or the free acetone derived from the diacetic acid, a strong stream of air, without heating or with heating over a free flame, is sucked through. The distilling glass contains 1-2 c.c. urine, 20-30 mg. oxalic acid, 0.5 gm. sodium chlorid and 5.0 c.c. distilled water, 15 c.c. hundredth-normal iodin solution and 1 c.c. 33% solution of caustic soda are put into the recipient tube.

To determine the free acetone a strong current of air is sucked through for twenty-five minutes, the recipient is changed for another tube prepared in the same manner and the air aspiration is repeated for fifteen minutes with heating of the distilling tube over a free flame. The contents in the recipient tube are acidified with hydrochloric acid and the nascent iodin is titrated up to the point of the disappearance of the blue coloration with hundredth-normal thiosulphate solution.

The following procedure was established for the determination of ammonia in the blood: 5 c.c. blood, rendered incoagulable by the addition of powdered 0.2% potassium oxalate, are diluted in a small graduated cylinder (holding 25 c.c.) with 0.1 c.c. tenth-normal sodium hydrate and the mixture is deprived of albumin by the addition of alcohol. The cylinder is filled up to the mark, the contents are well mixed and rapidly filtered into a dry vessel into which 1 drop of dilute sulphuric acid is placed for the binding of the ammonia; after alkalination with sodium carbonate solution, 20 c.c. of the filtrate are distilled off in the manner previously described in the water bath at 40° and under strong air suction. Before that, 2 c.c. fiftieth-normal sulphuric acid was placed into the recipient; methyl red was used as indicator and retitration was done with fiftieth-normal sodium hydrate solution. The distillation lasts fifteen minutes.

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**A Rapid and Accurate Method for Calcium in Urine.**

*Alfred T. Shohl and Frank G. Pedley, J. Biol. Chem., 50:537, Feb., 1922.*

The details of the method of Shohl and Pedley are as follows: To (Sec. 1—Page 649)

100 c.c. of unfiltered urine in a 250 c.c. Erlenmeyer flask add 5 c.c. of concentrated nitric or sulphuric acid, and 3.0-4.0 gm. of ammonium persulphate. Insert a funnel in the flask to prevent spattering. Boil and keep near the boiling point on a hot plate for one hour, or until the reduction of the ammonium persulphate is complete, as evidenced by an absence of frothing when the flask is agitated. The solution at this point is pale green in color. Add 10 c.c. of 2.5% oxalic acid. Neutralize with ammonium hydroxid, using 1 drop of methyl red as an indicator. Cool to room temperature and if the color is now red, the solution may be brought to the desired color by a few drops of ammonium hydroxid (pH 4.8 to 5.2). Let stand over night and then filter. Wash the precipitate and flask 3 times with distilled water, filling the filter  $\frac{2}{3}$  full each time and allowing to drain. Break a hole in the filter paper, and wash back the precipitate into the original flask, first with distilled water, and then with hot dilute sulphuric acid, bringing the volume to about 100 c.c. Add 10 c.c. of concentrated sulphuric acid, and heat to 70-80° C. Titrate with 0.05 N potassium permanganate, taking as an end-point the first color that persists fifteen to thirty seconds. If, as occasionally happens, the precipitate is colored red by the methyl red, and so colors the solution to be titrated with permanganate, this color does not interfere with the end-point as it is quickly oxidized. The indicator is not present in sufficient amount to cause any appreciable difference in the titration. The usual precautions should be taken of standardizing the permanganate each day with standardized oxalate. One c.c. of 0.05 N KMnO<sub>4</sub> equals 0.001 gm. or 1 mg. of calcium. The authors say this method requires less than  $\frac{1}{4}$  the time necessary for gravimetric determinations.

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(1b-93)

**The Effect of Hydrogen Ion Concentration upon the Determination of Calcium.**

*Alfred T. Shohl, J. Biol. Chem., 50:527, Feb., 1922.*

The following method (McCradden's) is the best for the accurate determination of calcium: Calcium is precipitated as oxalate in the presence of sufficient ammonium chlorid to hold the magnesium oxalate in solution, and of sufficient acid to hold the calcium oxalate partly in solution. Sodium acetate is then added to decrease the acidity and to precipitate the rest of the calcium oxalate on the crystals already formed. Thus, large crystals are made which are easy to filter and are not contaminated with occluded magnesium or calcium phosphate. The amount of acetate is selected so as to give a solution not acid enough to dissolve the calcium oxalate, nor alkaline enough, if cold, to allow calcium phosphate to precipitate. Shohl has critically examined McCradden's method in relation to pH. He (Shohl) determined the most acid limit, the point at which calcium oxalate begins to be converted into the more soluble acid calcium oxalate, and the least acid limit, the point at which magnesium ammonium phosphate and magnesium hydroxid precipitate. In regard to the best method of obtaining the desired acidity the author states that when sodium acetate is added to a mixture of hydrochloric and oxalic acids, the stronger acids form salts with sodium and there remains in the solution acetic acid in the presence of acetates. This is an excellent buffer mixture

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and regulates the pH. If one knows the ratio of the acetic acid to the sodium acetate, with Walpole's chart, one can estimate the pH. If the solution is more acid than pH 4.0 calcium oxalate is dissolved. If the solution is less acid than pH 5.6, magnesium ammonium phosphate is precipitated.

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Further Discoveries in the Use of the "Silver Method" for the Determination of Acetaldehyd, Its Usefulness for Determining Other Aldehyds, and a Convenient Way of Obtaining Acetaldehyd and Other Volatile Substances from Body Fluids.

Robert Fricke, *Hoppe-Seyler's Ztschr. f. physiol. Chem.*, 118:241, Berlin, Jan. 25, 1922.

The well-known Tollens aldehyd reaction is designed for the quantitative analysis of acetaldehyd. It is best carried out in the following manner: One treats the solution of acetaldehyd obtained by distillation with not too large an excess of N/10 silver nitrate solution, adds somewhat less N/10 NaOH and carefully adds ammonia up to the exact point of solution of the silver oxid produced. The solution is left to stand over night in the dark, then carefully heated on the return condenser and boiled for one minute. The solution is then cooled, treated with ammonia, the precipitate washed, the filtrate made acid with nitric acid free from nitrate, treated with ammonioferric alum solution and with N/10 ammonium thiocyanate solution titrated back against the original quantity of silver nitrate used. To each cubic centimeter of the N/10 silver nitrate solution which is used up, 2.2% acetaldehyd correspond.

This may also be utilized for the quantitative study of the homologues of the acetaldehyds, insofar as they are soluble in water. In order to obtain the acetaldehyd from body fluids, the steam distillation method is recommended. Although the acetaldehyd is not especially volatile with steam, it, by the very virtue of its extraordinary volatility, leaves the solution concerned with the first portion of the escaping steam. For quantitative distillation, it is sufficient to distill over one-tenth of the original volume. This method of isolation may also be employed for other constituents of body fluids, which are easily volatile or volatile by means of steam.

(1b—95)

The Detection of Aldol in Diabetic Urine.

Robert Fricke, *Hoppe-Seyler's Ztschr. f. physiol. Chem.*, 118:218, Berlin, Jan. 25, 1922.

Attempt has been made to detect the aldol which, as a connecting link between acetaldehyd and b-oxybuteric acid, should be present in diabetic urine. For this purpose, 54 liters of acid diabetic urine from very severe cases were distilled in steam, whereby the distillate containing the croton aldehyde formed from the aldol when heated to boiling (each time one-tenth of the quantity of urine used) was collected in a receiver containing a few drops of acetic acid. The distillates were united, 0.3 gm. dimedon (dimethylhydroresorcin) dissolved in 3 c.c. 80% alcohol were added, and the solution was allowed to stand over night in order to allow time for the formation of the con-

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ensation product between the aldehyd and dimedon. On the next day the acetone was removed on the water bath, the white precipitate filtered off, and the filtrate evaporated to dryness; the residue, when extracted with 80% alcohol, showed on addition of NaCl, no further precipitate. The precipitate previously obtained was extracted with ligroin to remove any acetaldomedon present, the residue was recrystallized and melted at the characteristic melting point (175° C.) of crotomedon; it did not give the iron chlorid reaction, which is given by all aldehyddimedon condensation products thus far known of melting point around 175°, such as: acrolein (183°), glyoxal (175°), para-oxybenzaldehyd (183°-184°), dimethylamidobenzaldehyd (185°), formaldehyd (187°-188°), benzaldehyd (193°), zimtaldehyd (193°-196°). All these give especially intense color reactions with iron chlorid. The crotomedon could, moreover, be distinguished from the glyoxaldimedon in that it is not soluble in benzol. Acetaldomedon and furfuromedon are, it is true, also soluble in ligroin, but they could not cause confusion, since the former melts at 139° C. and the latter at 150° C., while the precipitate had a melting point of 165° after drying. Therefore, it was established that crotonaldehyd may be obtained in small quantities from an acid diabetic urine through steam distillation, and that it may well have its origin only in the slight traces of aldol contained in the urine. A connection between acetaldehyd and  $\beta$ -oxybuteric acid through the stage of aldol cannot yet be stated with certainty.

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(1b—96)

**The Physiology of the Phenols. I. A Quantitative Method for the Determination of Phenols in the Blood.**

*K. F. Pelkan, J. Biol. Chem., 50:491, Feb., 1922.*

Pelkan's method is as follows: 10 c.c. blood are added to 50 c.c. distilled water in a 100 c.c. Erlenmeyer flask; 10 c.c. of 10% sodium tungstate and 10 c.c. of a  $\frac{2}{3}$  N sulphuric acid are added; the flask is closed and vigorously shaken for a few seconds. To precipitate the proteins completely 10 c.c. of aluminum cream are added and the flask is again shaken. The contents are transferred to a 100 c.c. centrifuge tube and centrifugalized for forty-five minutes. The supernatant fluid is filtered to the 45 c.c. mark in a narrow 50 c.c. graduate, 5 c.c. of a 5% solution of silver lactate in a 5% lactic acid are added, and the graduate is well shaken for one minute. After centrifugation and filtration, the filtrate is ready to be examined for phenols. This last step is carried out as follows: only 2 narrow test-tubes are required—one graduated at 15 c.c. and the other at 10 c.c.—in which both the total and the free phenols are determined. Thus, any error due to the graduation of 2 sets of test-tubes is avoided. The procedure for the determination of free phenols is this: the 15 c.c. tube is filled to the mark with the filtrate, 1 c.c. of the phenol reagent is added and the tube is shaken. (The phenol reagent contains 100 gm. sodium tungstate, 20 gm. phosphomolybdic acid, 50 c.c. phosphoric acid 85%, 100 c.c. concentrated HCl. This is gently refluxed for two hours with 750 c.c. water, and at the end of the period of heating made up to 1,000 c.c.). The excess silver precipitates out, the solution is filtered to the mark into the 10 c.c. tube, and 5 c.c. of 20% sodium carbonate are added. This solution is now transferred to another test-tube in which

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the color develops to its maximum in about twenty minutes. The 2 graduated test-tubes are meanwhile used for the determination of total phenols. The 15 c.c. tube is again filled to the mark with the same filtrate, 5 drops of concentrated HCl are added, and the tube is placed in a water bath at 100° C. for ten minutes. Boiling of the contents of the tube is avoided and no loss of volatile phenols occurs, as the author showed by repeating the determination with known amounts of phenol. If the tube has a diameter of 14 to 15 mm., the volume of the contents on cooling at the end of exactly ten minutes is back to the graduation mark, so that no adjustment of volume is necessary. Then 1 c.c. of the phenol reagent is added and the solution is treated in the same way as in the determination of free phenols. The difference between the total phenols and the free phenols represents conjugated phenols. The standard is prepared as follows: 5 c.c. of a stock solution of resorcinol containing 5.81 mg. are placed in a 100 c.c. volumetric flask; 0.5 c.c. of concentrated HCl and 10 c.c. of the silver lactate-lactic acid solution added; the mixture is centrifugalized or filtered; and the filtrate is manipulated in the graduated test-tubes in the same manner as the blood filtrate in the determination of free phenols.

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**The Physiology of the Phenols. II. Absorption, Conjugation and Excretion.**

*K. F. Pelkan and G. H. Whipple, J. Biol. Chem., 50:499, Feb., 1922.*

Pelkan and Whipple studied the factors concerned in the normal and abnormal metabolism of phenols in that body, directing particular attention to the liver. Dogs weighing 20-35 lb. were used in these experiments. The mixed diets employed contained a liberal amount of table scraps including cooked meat, macaroni, potatoes, bread and bones. It was necessary to control diet factors in these experiments because of the observations of previous workers to the effect that urinary phenols vary directly with the protein intake, and with an increase in output of total phenols the percentage of free phenols remains constant. The most important volatile phenols present in the body are p-cresol and phenol and the experiments were therefore limited to these 2 substances, attention being focussed upon p-cresol, since it was found that complete conjugation occurs with it more rapidly than with any other phenolic substance investigated. At first known amounts of phenol in a watery solution were injected into the jugular vein of the animal and the blood drawn just prior to and at stated intervals after the injection was analyzed for total and free phenols. Later the intravenous method was abandoned and the phenols were administered to the animals via a stomach tube. The latter method is more satisfactory since it does not produce such violent toxic symptoms in the animal. From the tabulated results one learns that intravenous injection of phenols is followed by a prompt and uniform distribution of such substances in the body fluids and tissues. Following such injection there is a rapid disappearance of free phenols from the blood and a rapid increase in conjugated phenols. This rise in conjugated phenols usually reaches a maximum within one hour and thereafter slowly declines with excretion. The authors also observed a uniform distribution of these conjugated phenols throughout the body fluids

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and tissues. Ingestion of phenols gives a different picture. With a sufficiently large dose some free phenols appear in the blood for a short period, rarely more than thirty minutes. The conjugated phenols show a maximum rise during the first and second hours and subsequent decrease due to renal elimination. The process of phenol metabolism is as follows: A small part of the tyrosin of the food proteins is broken down by bacterial action into hydroxy-acids, such as p-oxyphenylpropionic, p-oxyphenylacetic, and p-oxybenzoic acids, and into volatile phenols, primarily p-cresol and phenol. The hydroxyacids which have no toxic effects are not subjected in any noticeable degree to oxidation or conjugation and are practically completely excreted in the urine in the free state. The volatile phenols which are very toxic even in small amounts are dealt with in an entirely different way. More than half of these toxic phenols are oxidized by the intestinal mucosa, body fluids, and liver parenchyma. The remainder are conjugated in the liver with sulphuric or glycuronic acids. After passing from the liver the conjugated phenols are uniformly distributed to all the tissues and are rapidly eliminated by normal kidneys probably within twelve hours.

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#### The Determination of Oxalic Acid in the Urine.

*E. Mislowitzer, Biochem. Ztschr., 126:77, Berlin, Dec. 27, 1921.*

According to Bau, his chalk acetate (Kalkessig) method is the most exact, simple and inexpensive method of determining the oxalic acid content. Bau precipitates the oxalic acid directly from the filtered urine with the aid of a mixture composed of sodium acetate, calcium chlorid and acetic acid which he calls chalk acetate. Since, however, small amounts of calcium oxalate always remain in solution, Bau compensates this error by the use of so-called constants based on the maximum solubility of calcium oxalate in urine and in the water employed for the washings. This method of Bau's was compared with the method of Salkowsky. Salkowsky's method is based on shaking the urine with ether and alcohol. The calcium oxid obtained by heating the calcium oxalate to redness was determined acidimetrically. The comparative experiments showed a considerable superiority of Sarkowsky's procedure, in particular if the duration of the individual shakings was prolonged and the volume of ether was increased. Sarkowsky's procedure was superior to Bau's method even if Bau's constants were added to the directly obtained figures. Instead of shaking by hand, the shaking of the urine should be done with the aid of the shaking apparatus. Bau's claim that the chalk acetate method is the most exact procedure is, therefore, not in accord with these results.

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#### The Action of Oxalic Acid in the Animal Body.

*Ludwig Pincussen, Biochem. Ztschr., VBFSRB, Berlin, Dec. 27, 1921.*

Under the action of light rays, the purin metabolism does not stop at uric acid and allantoin, but chemical decomposition proceeds down to oxalic acid. Since, however, the oxalic acid under the influence of the light is further broken down rapidly, it must be assumed that part of

the oxalic acid is still further oxidized. Consequently, opinions are divided on the question of whether oxalic acid is in all cases the end-product of animal metabolism. To clarify this problem, oxalic acid obtained from the sodium salt was injected subcutaneously in 1% solution into rabbits. It seems that frequent injections of oxalic acid, on account of the withdrawal of calcium caused by the oxalic acid, has a distinct influence on the resistance of the animals. As source of light, a carbon arc-light was used; eosin sodium dichloranthracenebisulphate served as sensitizers. The experiments show that under ordinary conditions, four-fifths of the oxalate appeared unchanged in the urine. In irradiated and sensitized animals approximately 33% less oxalic acid is excreted than without irradiation. These experiments show that in the rabbit organism, under ordinary conditions, oxalic acid is to be considered the end-product. Upon increased oxidation under the influence of light rays, the combustion goes even further. Carbonic acid and water must be regarded as the end-products of the oxydation.

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**The Detection of Small Quantities of Lead in the Urine.**

*O. Schumm, Hoppe-Seyler's Ztschr. f. physiol. Chem., 118:189, Berlin, Jan. 25, 1922.*

In connection with the secretion of lead in the urine and recognition of lead-poisoning, various procedures were tested. The precipitation of lead as lead sulphid from urine treated with hydrochloric acid and potassium chlorid has not yet been confirmed. Experiments were undertaken for electrolytic separation of the lead, whereby the organic substances were treated in the urine partly with nitric acid and partly with potassium chlorid and hydrochloric acid. From these experiments it was shown that these methods were not very satisfactory as regards small amounts. Therefore, the electrolytic separation of small amounts of lead was attempted in various ways: by dissolving in nitric acid alone, by dissolving in nitric acid with the addition of potassium and sodium chlorid, then with the addition of copper sulphate; then by precipitation of the lead from urine containing lead and treated with copper sulphate, by hydrogen sulphid and electrolytic extraction of the lead from the sulphid combination. It was shown that the lead, by the use of small platinum plate electrodes, is quite well separated by an electrolysis of 4 volts, from strong nitric acid solutions which contain from 0.3 to 0.1 mg. lead nitrate (dilution 1:65,000-1:200,000). The most of it does not, however, regularly appear on the anode as lead peroxid, but sometimes on the anode and sometimes on the cathode, according to the conditions of the experiment. Therefore, with quantities of 0.1 mg., attention must be given to both anode and cathode. As anode a flat electrode plate was used, with about 3 sq. cm. of effective surface. As cathode there may also be used effectively a polished platinum plate instead of the platinum electrode. In cases when the nitric acid content is high the electrolysis must be continued longer, as the length of the electrolysis is determined, with the same current, by the amount of nitric acid present. In the presence of larger quantities of potassium or sodium colorid, the lead, even in a dilution of 1:70,000, is not separated on the anode from a strong nitric acid solution by the described experimental process in sufficient quan-

tity to give certain proof, so long as the chlorin action persists. If the electrolysis is continued until the total disappearance of the chlorin, an altogether satisfactory separation of the lead may be obtained. The uncertainty of the lead proof in urine treated with nitric acid or with potassium chloride is conditioned by the presence of alkali chlorides in the urine and is an argument against this process. For the detection of small quantities of lead in the urine, the process recommended by Meillère is suitable. The electrolytic separation, necessary in this case, of the copper from the lead, was successfully accomplished without extra heating by using a small platinum plate as cathode and a platinum plate electrode, polished smooth or treated with aqua regia, of 3 sq. cm. effective surface, as anode. The force was 4 volts with an initial current of 0.5 ampere. The electrolysis lasted twenty hours. The combination of about 15 c.c. 25% hydrochloric acid and 0.4 gm. copper sulphate to 1.5 liter was used, with the introduction of hydrogen sulphide at 40°-50°C. for one-quarter hour. The nitric acid extract of the hydrogen sulphide precipitate may be electrolyzed at once after concentration and dilution with water. It is best to bring the extract of the hydrogen sulphide precipitate to a red heat, in order to dry it by evaporation, to treat the residue with warm dilute nitric acid and quickly separate the lead by electrolysis. It is recommended to use only a little nitric acid (6-10% nitric acid). Urine containing a slight amount of albumin may also be handled in the same manner, at times, without difficulty. A larger amount of albumin inhibits the procedure. If the combination of copper sulphate, as recommended by Meillère, is omitted, and the hydrogen sulphide has a moderate acid content, a small quantity of lead will remain undetected.

The test given by Lewin (boiling a mixture of urine and egg albumin in potassium lye) is not suitable for the detection of traces of lead in urine, as considered in this article.

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**A Changed Type of Saccharometer.**

*Lassar Cohn, Deutsch. med. Wchnschr., 48:95, Berlin, Jan. 19, 1922.*

A change of the known Einhorn's apparatus: The limb which is usually closed may be opened or closed with a glass stopcock and is marked off on a scale which gives the number of c.c. of CO<sub>2</sub> formed. The other limb has a receptacle for catching the CO<sub>2</sub> which develops from the urine and which runs over.

A table is used in the determination of the percental content of sugar. Urine which contains more than 0.8% must be diluted in the accessory tube. It is easy to clean the apparatus.

The manufacturers are Greiner and Fredrichs, Stützerbach in Thüringen.

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**Physiology of the Polyamyloses. I.**

*Hans Pringsheim und Karl O. Müller, Hoppe-Seyler's Ztschr. f. physiol. Chem., 118:236, Berlin, Jan. 25, 1922.*

The products designated as polyamylose were the crystallized sugars obtained from starch by means of *Bacillus macerans*, and their  
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depolymerization product derived chemically. The explanation of the rôle of the polyamyloses, in starch and glucose formation, may possibly be found by the systematic formation of starch in chloroplasts freed from starch by absence of light. By this method, positive results were obtained in the case of various plants. For the tests, Spirogyra dubia were cultured in tap-water. After from eight to eleven days the fibers were freed from starch. These starch-free fibers were placed in the solution to be tested in a dark room and left there for five days. Every twenty-four hours, fibers were taken from the cultures and tested for starch with an aqueous Gram's solution. The table of experimental results indicates that the polyamyloses alone were not adapted to the formation of starch. Besides the monosaccharids, glucose, fructose, galactose, maltose (which is more closely connected with starch), and also glycerin, were adopted to starch formation. The sugar alcohols were not starch builders; but from them, apparently, starch is formed only in the plants which depend upon it especially, as, for example, the oleaceae depend upon mannite, the Rosaceae upon sorbite, and Adonis vermalis upon adonite.

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**The Production of Ferments in the Cell.**

*Martin Jacoby, Klin. Wchnschr., 1:184, Berlin, Jan. 21, 1922.*

Certain bacteria, e.g., proteus bacteria, grow upon liquid nutrient media which contain some more or less indispensable salts and only very few organic substances. Cultures are obtained in this way which can be examined as to their effects upon fermentation and they can even be used for the preparation of ferments. In order to be able to study the formation of ferments, 2 different types of products may be added to these cultures: (1) the type which increases considerably the already-existing production of ferments; or (2) another type which induces the cells to produce ferments which could not have been formed without the addition of these substances. Carbohydrates are the most important substances of this kind. Their significance in promoting the formation of ferments can be studied best when using ferments which by themselves do not decompose carbohydrates. This avoids the double action of carbohydrates as promoters of the production of ferments and as substrates. (The substrates probably influence the formation of ferments.) The investigated ferments were ureases, which decompose urea into carbon dioxid and ammonia, and catalases, which decompose hydrogen peroxid into water and oxygen. It is a well known fact that the molecules of different carbohydrates contain a different number of carbon molecules. The most important ones among them, as far as their influence upon the formation of ferments is concerned, are those which have a molecular chain of 3 or 6 carbons. This is probably not an accident. Apparently the substance of cells is provided with groups which can react directly with these particular carbohydrates. As the carbohydrates are not indispensable for the formation of ferments, but simply considerably increase their production, it may be assumed that they have only a stimulating effect upon the formation of ferments. It is quite possible that the building materials of the ferments exist in the cells independently of the carbohydrates and that their formation only proceeds more rapidly in the presence of carbohydrates. In the case of amino-acids it is necessary to make some

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differences. A certain amount of amino-acids is absolutely necessary for the formation of ferment, and it is unimportant to know whether amino-acids influence the formation directly or indirectly. If they acted directly it would mean that the cells produce ferment with their direct help, while otherwise the cells are put in a condition which enables them to form ferment. Different amino-acids can fulfill these requirements, but besides these quantitative functions certain amino-acids are connected with some qualitative action of the cells. This fact, which is of highest importance for the formation of ferment, is a most significant phenomenon from a biologic point of view. What is important for the formation of ferment, is also important for the formation of other component parts of cells. This explains why albumin, one of the main components of protoplasm, is not composed of chains of similar amino-acids.

The growth of proteus bacteria in simple, chemically known nutrient fluids was investigated. These cells may be allowed to increase abundantly in numbers, without any danger of their producing urease. Only under one condition was it possible to force the bacteria to form this ferment, namely, by the addition of leucin. Of course, it cannot be said that leucin might not be replaced by some other products. In any event, the formation of urease took place only when leucin, which was obtained from albumin, was added, while the synthetic product remained without any effect. It can be easily recognized that in this case the amino-acids have a special function which resembles the functions of vitamins. Consequently, it is possible to influence bacteria in such a manner that they either produce a certain ferment or not. The experiments further show that the bacteria formed catalase.

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**The Stimulators of the Alcoholic Cleavage of Sugar. The Chemically Defined Catalysts of Fermentation.**

*Carl Neuberg and Marta Sandberg, Biochem. Ztschr., 125:202, 126:153, Berlin, Dec. 8, 27, 1921.*

A series of pronounced chemically definite catalysts of alcoholic splitting of sugar have previously been extensively examined, including  $\alpha$ -ketones, aldehydes, ketones, diketones, disulphids, nitrogen-oxygen combinations, reducible mineral substances. In this work, those belonging to the purin group were also tested in this respect: the yeast juices were tested, so that the objection, that they may have some indirect action on the living cell, cannot be raised. As the vitamins have not been prepared in a pure state and are unclassified in respect to their functional group, it must be mentioned that they contain more or less abundant representative body-groups known as enzyme stimulators. The investigations were conducted with yeast strains of surface fermentation. The activator effect should be determined in all the strains, even if they show gradual differences. The attained acceleration of carbonic acid liberation reaches the proportion of several 100%, in comparison to the activator-free controls. Yeast strains of deep fermentation were not tested. Of the lower purin derivatives, not only the natural products, but also the combinations derived from synthesis were used, so that adherent foreign bodies of vitamin nature could be excluded with certainty.

The experiments showed that the purins stimulate the transposition of the sugar through the fresh fungi, not only in the free state, but also in higher molecular combinations, and also in the form of decomposition stages. Adenin and guanin act admirably, not only in themselves but also in the form of salts; hypoxanthin, xanthin, 8-methylxanthin, tetramethylxanthin and theobromin act well; the substitution products trichlorotetra xanthin and tetrachlorotetramethylxanthin, also the nucleic acids, both of vegetables and animal origin, as well as the decomposition products of purins—alloxanthin, mesoxalic acid, allantoin, barbituric acid and paraban acid act favorably; heteroxanthin was less active and aloxan and inosin acid, which were tested as barium salts, inhibited the enzyme action, and caffeine was inactive. The cause of the latter group's action lay in the fact that these can partly transpose themselves and that peculiar physiologic relationships exist to parts of the living cell. Altogether, the experiments showed that the purin group and their derivatives are effective as activators of alcoholic splitting of sugar.

In the technical explanation of the fermentation process with living yeast, the bitter principles come into question. Such chemically defined substances as absinthin, cetratin, cubebin, elaterin, peudeanin, picrotoxin and aloin were tested for their influence on furthering fermentation. All proved to aid fermentation, although aloin and picrotoxin were very weak. Quassain showed itself refractory. The series of experiments were performed in such a way that to 10 cm. fresh yeast there were added 5 c.c. yeast suspension (2.5 gm. in 100 c.c.), 5% glucose solution and 0.05 gm. activator. In testing with yeast juices 15 c.c. yeast juice, 1 c.c. 25% glucose solution and 0.05 gm. activator were combined. In each case, a control without activator was performed. Experiments were also tried with substances of high molecular weight from the aromatic series, which may have some effect; their action in this connection was tested. Here belong abietin, apocholic, cholic, and desoxychloric acid, which showed themselves in a free state to be stimulating to fermentation but inhibitory when in the form of their sodium salts. In the fermentation of the fresh yeast only a slight influence was revealed by the coupled gallic acids such as glycocholic and taurocholic acids. Cholic, copaibic, naphtha and sylvan sodium salts were found to be inhibitory. An important hastening, also, of the cell-free fermentation with carbon, bone-black, charcoal, could be shown in yeast juices of different origin. This may be due to the fact that with the addition of phytochemically reduced substances of organic or inorganic origin, the acetaldehyd is to be considered as a primary oxidation equivalent. Of the saponins, it could be ascertained that quillaja saponin, beet saponin and beet resinic acid hasten fermentation in the same manner. Digitonin and digitalin inhibit in the use of fresh yeast, while they hasten considerably, as does cyclamin also, in the use of juices. Pure cystin, as also a polypeptid rich in cystin and keratin made into solution, showed important stimulative results when fresh yeasts were used, apparently because they are especially good hydrogen receivers and the disulphid group is thereby activated. The mechanism of the hastening of fermentation may not yet, however, in the light of the experiments, be considered as explained and may be connected with the problem of phytochemic reductions.

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**The Detection and Identification of Maltose, Galactose, Saccharose and Inulin, by a Mycologic Method.**

*Aldo Castellani and Frank E. Taylor, J. Trop. Med. & Hyg., 25:41, London, Feb. 15, 1922.*

The method, which the writers describe, to determine whether a substance is or is not a certain carbohydrate, is to test on the substance 2 germs known to be identical in all their fermentative reactions except on that particular carbohydrate. The following method of procedure in which maltose is used for example was used to identify galactose, saccharose and inulin:—A 1% sterile solution in sugar-free peptone water is made of the substance to be identified. This solution is distributed into tube No. 1 which is then inoculated with *Monilia tropicalis*, and into tube No. 2 which is inoculated with *M. macedoniensis* or other monilias of the same group. These are incubated for four days at 37° C. and if No. 1 contains gas and No. 2 does not the substance is maltose, for *M. tropicalis* ferments with production of gas only glucose, levulose, maltose, galactose and saccharose; while *M. macedoniensis* ferments with the production of gas, glucose, levulose, galactose, saccharose and inulin. If the substance had been either one of these sugars *M. macedoniensis* would have fermented it and gas would have been produced, therefore the substance must be maltose. Further, similar tests are made to prove the identity of the substance with *M. pinoyia*, *M. metaloridinensis* and *M. krusei*.

Generally it is believed that there is no fungus which induces complete fermentation of inulin, but Castellani found that *M. macedoniensis* Cast. and allied species, caused complete fermentation with large production of gas. A table containing the fermentative character of the various fungi and bacteria used in the mycological method is given and also a list of the principal mycological formulas which the writers devised and employed in the identification of various sugars and other carbon compounds. Strains with permanent biological reaction must be used. Acid fermentation without production of gas was not taken into account.

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**The Mutarotation of Dextrose under the Influence of Sodium Chlorid (the Mutarotation as Analytic Method).**

*Hans Murschhauser, Biochem. Ztschr., 125:158, Berlin, Dec. 8, 1921.*

The process of mutarotation of dextrose, which occurs in the purest distilled water at a temperature of 20° with a definite rapidity, is hastened by the addition of acid or alkaline reacting substances: the greater the amount of the solution to be examined for the particular catalyst, the greater the rapidity. The hydrogen and hydroxyl ions controlling the reversed rotation and, parallel with it, their concentration, increases the rapidity constant of the reaction. In regard to the effect of salts upon the reversed rotation of dextrose solutions, it was previously known that sodium chlorid exerts an inhibiting effect, but the other salts show a hastening effect. The neutral salts examined were sodium sulphate, potassium nitrate, potassium iodid, ammonium chlorid and barium chlorid. According to other investigations, neutral salts are supposed to have no effect upon the reverse rotation.

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Proceeding from the recognition of the fact that the previous experiments gave no clear picture only because the salt concentration was not sufficiently high, the latter was increased up to the limits of saturation and with this solution the experiments were conducted. Descending from this concentration the dilution was carried down to pure distilled water. Repeated readings were made for the sake of accuracy.

A table shows that the rapidity constants of the mutarotation with water are not influenced in such a way by sodium chlorid in amounts of 0.1, 0.02, 0.01, 0.002 and 0.001 molecular weight that their amount can be determined with certainty: only with the  $\frac{1}{2}$  molecular weight is the clearness definite and this increases with the increase of salt in the solution. The quantitative relation between the salt concentration and rapidity constant is seen more distinctly when the effect of the salt is isolated to the course of the rotation and the difference between the constant for the watery solution and that of the different salt solutions is obtained: the rapidity constant of the course of the mutarotation of dextrose diminishes in proportion to the increase of the concentration of the sodium chlorid.

The mutarotation can also be used as an analytic method for the recognition of the purest sodium chlorid, as it is well known in what manner and to what extent the purest sodium chlorid influences the rapidity constant of the mutarotation of dextrose. The reverse rotation of a watery dextrose solution is hastened in a more or less high degree by all substances with the exception of sodium chlorid: acid and alkaline reacting substances act the strongest and neutral reacting salts show very slight hastening. As the effect of sodium chlorid upon the mutarotation is definite only in highly concentrated solutions and impurities can be present only in a very small percentage, a result can only be expected from the use of high concentrations: the concentration of 4 molecules per liter may serve as a groundwork for this determination. From these examples the conclusion can be drawn that the mutation procedure is well fitted for the demonstration of extremely minute amounts of sodium chlorid (which do not show with any other method) as is no other method, and also that a quantitative determination of these impurities is possible by the amount of increase in the rapidity constant.

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Influence of Sodium Chlorid on the Mutarotation of Dextrose in Hydrochloric Solution.

Hans Murschhauser, *Biochem. Ztschr.*, 126:40, Berlin, Dec. 27, 1921.

In a series of experiments on the influence of the sodium chlorid on the mutarotation of dextrose in aqueous solution it was found that the velocity constant of the reversal of the rotation decreases in a straight line with an increase of the NaCl concentration of the solution. The experiment shows that the NaCl in acid solution has an action on the mutarotation of dextrose different from that of NaCl in neutral solution. This observation led to the attempt to study in a more extensive manner the influence of NaCl on the mutarotation of dextrose. Two problems were to be considered; (1) in what sense and to what degree addition of varying amounts of NaCl would influence the velocity of the mutarotation of dextrose in HCl of a certain concentration (Sec. 1—Page 661)

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tion; (2) if the charge of the velocity constant produced by the addition of a definite amount of NaCl would be the same for all concentrations of the acid.

A 4N solution of NaCl and an approximately 0.1N HCl solutoin were employed in the experiments. The temperature was 20.4; 5 gm. dextrose were dissolved in the solvent and enough of the solvent added to make up 100 c.c. of the solution; the angle of rotation X corresponded to a tube length of 189.4 cm.; the velocity constant of the reaction calculated from the above value by means of  $\log b - \log (b-x)$  was denoted with C. The water was distilled over sulphuric acid with potassium permanganate and over baryt. The experiments were carried out with varying salt content in decreasing concentration and the results were recorded in tables and curves. The experiments showed that the velocity constant of the mutarotation of dextrose dissolved in an approximately 0.1 normal HCl is accelerated upon addition of NaCl; the value of this acceleration increases in a straight line with an increase of the NaCl concentration.

The quantitative difference existing between the retarding effect of NaCl in neutral solution and the accelerating effect of the same salt in acid solution may be seen from the following figures. NaCl—concentration; 4.5, 4, 3, 2, 2, 0.5, 0.1, 0.05, 0.02, mols. Retardation of mutarotation in salt-free aqueous solution: 4.1, 3.6, 1.7, 0.82, 0.4, 0 units. Acceleration in 0.1 normal HCl: 15.6, 16.9, 10.35, 7.1, 3.6, 1.7, 0.65, 0.3, 0.1 units.

Hence the accelerating effect of NaCl in acid (0.1 N HCl) solution is approximately 4 times as large as the retarding effect in neutral solution. This fact explains why in acid solution already an addition of 0.1 N and 0.2 N NaCl produces a deviation as compared to the salt-free solution, while in a neutral solution an addition of 0.5 N NaCl is required to produce a distinct retardation.

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### **Signs of Poisoning in Amylases.**

*Urban Olsson, Hoppe-Seyler's Ztschr. f. physiol. Chem., 117:91, Berlin, Dec. 5, 1921.*

This investigation supplements earlier communications. Iodin was employed for poisoning malt amylase. The action of potassium iodid was tested and regeneration of the enzyme was attempted by means of sodium thiosulphate. The poisonous action of potassium iodid was minimal in comparison to that of iodin and it was shown that thiosulphate was unable to regenerate the enzyme although an experiment demonstrated that the diastatic power of the enzyme could not be reduced by thiosulphate. It was not possible to regenerate malt amylase poisoned by iodin with anilin. The attempts to regenerate by means of thiosulphate and anilin show, however, that iodin is strongly linked to the enzyme molecule and can not be liberated from the same as readily as from starch.

In a second series of experiments the poisoning of malt amylase by aldehyd reagents was studied. Malt amylase lost 30-90% of its original diastatic power within from 10 minutes to over 32 hours at 37° C. Phenylhydrazin exhibited the strongest action. Analogous poisoning experiments were undertaken with oxidizing agents and malt amylase

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was found to lose its diastatic power gradually in ammonium molybdate and sodium tungstate solutions. Metallic salts were then tried and, owing to the close relationship between uranium and the foregoing metals, uranyl sulphate was tested first. In this case, too, malt amylase lost 57% of its original activity relatively quickly. The action of sodium chlorid showed that the fluorin ion and iodin ion do not poison malt amylase, but that the poisonous action is always due to free iodin. Having regard to the general presence of the iron ion in the animal and vegetable organism, experiments were made with ferric chlorid. It appeared that activation of the enzyme took place with weak concentrations of this, whereas stronger concentrations caused poisoning. Analogous experiments with zinc sulphate, which is also a constituent of the animal body, did not show the same anticipated activation of malt amylase with low concentrations, in spite of the very wide concentration interval. In mercurous nitrate, calomel and mercuric chlorid, malt amylase lost up to 90% of its diastatic power. Of the amino-acids (leucin and alanin) only alanin acted strongly, while leucin acted in weak concentrations, but after more prolonged action no enzyme poisoning worth mentioning was observed.

As malt amylase and salivary amylase are not identical, it was assumed that they would show differences in poisoning experiments not ascribable to differences in purity or to the presence of the regenerative materials. An enzyme solution was prepared by shaking 175 c.c. human saliva ten minutes with 2 gm. kaolin, and filtering immediately. Toluol having been added, the filtrate was dialyzed five minutes through collodion membranes against distilled water which was renewed occasionally. Phosphates and chlorids appearing to be probable activating agents of salivary amylase, experiments were made with sodium phosphate; this increased the enzymatic activity only 17%. A corresponding amount of sodium chlorid, however, gave an increased activation of 277%. The activating influence of the external liquid in salivary amylase dialysis was also detectable, malt amylase being activated 10% and salivary amylase 104%. The investigation of the bearing of the concentration on the activation of salivary amylase showed that with a sodium chlorid solution possessing the normality of 0.017 in the activator retort, or of 0.0011 in the reaction retort, 46% of the diastatic power of the undialyzed enzyme solution was regained and that the dialyzed enzyme solution could be activated 375%.

Further, it was sought to determine the reaction optimum of salivary amylase in the simultaneous presence of sodium acetate and sodium chlorid. The reaction optimum of salivary amylase was found at pH=6.4 and the concentration of the sodium acetate solution was then 0.065 in the reaction retort, that of sodium chlorid being 0.0021 normal. In the researches on poisoning of salivary amylase that followed, these concentrations were employed. The poisoning agents were iodin, anilin, formaldehyd and copper sulphate. Free iodin exercised a powerful poisonous action on salivary amylate, anilin, formaldehyd and copper sulphate being less effective. The experiments demonstrated a dependence of poisoning on temperature. The experiments on copper sulphate poisoning were conducted at different temperatures and the results compared with those given by mercurous nitrate, hydroxylamin, ammonium molybdate, sodium tungstate and anilin. Usually poisoning of malt amylase and salivary amylase increases with time but tables

show great differences with the different poisons. Thus, copper sulphate poisoning increases very rapidly with time and reaches its maximum within half an hour. Mercurous nitrate and iodin poison instantly. Salivary amylase is less sensitive to light than malt amylase, which points to an absolute difference of these enzymes. By dialysis an activator is removed from salivary amylase, which probably consists of salts requisite for the diastatic action. For the determination of otherwise analytically indeterminable quantities both malt amylase and salivary amylase may be employed.

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**The Reducing Power of Cow's Milk Diastase on Various Kinds of Starch.**

*Ferdinand Welzmüller, Biochem. Ztschr., 125:179, Berlin, Dec. 8, 1921.*

Ferment reactions were used in the examination of the milk and oxydases and reductases were demonstrated. The views of different authors regarding the power of milk to show a diastatic effect are contradictory. As criteria which can be used for comparison of the diastatic action of cow's milk with that of diastases of other origin, the optimum temperature and the effect upon the different kinds of starch can be used. The ability of fresh milk from healthy cows to reduce starch was tested on wheat, maize, potato, arrow-root, sago, corn, barley, starch, oat, bean, pea, both cultivated and wild chestnut and buckwheat; a water-soluble starch was prepared from these according to the directions of Lintner. The water-soluble starch was boiled down to 0.5% paste. Each of 12 test tubes containing 10 c.c. milk was charged with a continuous series of 1, 2, 3, 4, etc. drops of the 0.5% paste: after thirty to sixty minutes' action an iodin solution (consisting of iodin, potassium iodid and water in the proportion of 1:2:300) was added; the tube was well shaken and the resulting color tone immediately determined. If the color of the fluid was yellow, the reaction was considered negative; if it was distinctly greenish, brownish, or bluish, the starch reaction was considered positive. If the reaction to starch with iodin as described was negative, it was assumed that all the added starch was split to low dextrins; the Allihn method was used to estimate the starch content of the paste.

The following conclusions were drawn from the tables computed: The optimum temnerature of the diastatic effect of cow's milk lies at about 37° C., at 42° C. there is a noticeable weakening of the diastatic ferment, which is further increased at a higher temperature. This shows that the diastase of cows milk is not similar in nature to that originating in malt or in the pancreas, whose optimum temperature is about 54° C.; the diastatic ferment of cow's milk easily reduces the starch of bean and pea and also of potato. Those graminaceae considered as easily digestible are more severely attacked. Although the experiments were conducted with previously treated starch, the controls, however, with previously untreated starches showed that the latter are reduced more more vigorously and less than those previously treated with cow's milk diastase. These inhibitions, however, did not appear with all the varieties of starch to quite the same extent, so that the relationship of the individual starches to one another, taken as a whole, was only slightly changed.

(1b—109)

(1b—109)

Lactase Content and Fermenting Power of Lactose Yeasts.

Richard Willstätter and Gertrud Oppenheimer, Hoppe-Seyler's Ztschr. f. physiol. Chem., 118:168, Berlin, Jan. 12, 1922.

It will be possible to determine the characteristics of the various races of yeast more completely than hitherto by means of their sucroclastic and fermentative enzymes when the quantitative analysis of the enzymatic processes can be carried out with the fungus itself. So far, the enzymatic activity of yeast in fermentation can be observed merely as a whole by measuring the fermentation process. The present communication deals with the question whether lactose is fermented directly by certain yeasts. The action of yeast lactase is optimal in a neutral medium. The duration of lactose decomposition deviates widely from the law of monomolecular reaction and corresponds entirely to the hydrolysis of maltose and glucosids by yeast enzymes. The action of lactase in three lactose yeasts, determined quantitatively in numerous cultures, differed widely, as shown by lactase time values of 3000-7. Great fluctuations were observed with approximately identical lactose yeast grown almost simultaneously. Differences arising from altered nutrition are explicable. The fermenting capacities of lactose, glucose and galactose are very unequal. Lactose fermentation with yeast of known lactase value shows no relationship between the yeast's lactase content and carbohydrate-splitting enzymes and zymases. The fermentation of lactose is obviously frequently preceded by decomposition but it is probable that lactose is fermented without decomposition. Lactose ferments more rapidly than the corresponding mixture of glucose and galactose, and this process is also more rapid than its hydrolysis by the same yeast under optimal conditions. If lactose fermentation be interrupted no monose is found, while in the fermentation of cane sugar the two components quickly appear in the sugar solution. The action of lactase was measured by the number of minutes required by 1 gm. dried yeast, or by the enzyme solution corresponding to this amount, to hydrolyze 2.5 gm. lactose at 30° and at optimal hydrogen-ion concentration in 50 c.c. solution. The most favorable hydrogen exponent was taken as 7. It is obtained with 10 c.c. phosphate buffer, in the proportion of 3.8 primary to 6.2 secondary salt. For all experiments hydrated lactose was employed. The mixtures of lactose and its components were tested by the copper method under Bertrand's conditions. As kefir seeds could not be obtained in a state fresh pure cultures of lactose yeast were utilized for lactase estimations. Saccharase may be estimated quantitatively in fresh yeast just as in aqueous solution. Willstätter and Steibelt's method of maltase estimation in yeast, which depends on rapid liquefaction of the yeast with destructive agents, neutralization of the acid formed and adoption of the most favorable hydrogen exponent, was found applicable to lactase and gave good results. The estimation was carried out so that 1 gm. fresh yeast of definite dried weight was triturated with 3-4 drops chloroform until liquefied. The yeast is then diluted in 5 c.c. water, neutralized with 1% ammonia and estimated quantitatively with lactose and buffer. The lactase values fluctuate and obviously depend on the yeast's physiologic condition. In any case they are influenced by conditions of nutrition and culture. Formerly it was considered that fresh (undried) yeast lost invertin but not maltase or lactase to

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water. That is not the case. Without drying yeast, lactase may be isolated from it by taking fresh yeast, liquefying it by triturating ten minutes with 1 c.c. chloroform, diluting with 7 c.c. water, neutralizing carefully with 1% ammonia and filtering two or three days later. The yield varies. The result from 0.8 gm. dry yeast was: experiment 90 minutes, copper 75.8 mg., decomposition 49%, time value 75. The variations in lactase fermentation may be explained by assuming that lactase, zymase (which ferments glucose) and a lactozymase fermenting lactose directly, occur together in yeast quite independently of one another, each in its own variable active amounts. In this connection fermentation experiments on the different sugars may be carried out simultaneously with the same yeast sample. The experiments were conducted under the conditions laid down by Willstätter and Steibelt, and showed that no relations exist between lactase content and the rapidity of lactase fermentation. In living fermenting yeast the action of lactase is not the same as in killed yeast. Either lactase is not present in living yeast to the same amount that was estimated quantitatively by the authors or it does not find those conditions in the living yeast cell under which it is subject to enzymatic hydrolysis and which were selected for the quantitative estimation. If lactose functions in fermentation, monoses should be present in the residual solution when yeasts rich in lactase are employed, and galactose should increase in the residual solution analogous to the increase of fructose in sucrose fermentation, but neither of these occurs.

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(1b—110)

**Yeast Albumin.**

*Alexander Kiesel, Hoppe-Seyler's Ztschr. f. physiol. Chem.*, 118: 304, Berlin, Jan. 25, 1922.

The albumin of yeast, after extraction by ether water and autolysis, was extracted by Schroeder from the pulp with water and separated from the filtrate by acidulation with acetic acid and heating. Later, the same method was tried by Thomas. All experiments made thus far were compared, and the following figures resulted:

	Schröder	Thomas	Kiesel	Thomas	Casein
Histidin	1.98	2.02	2.97	2.63	
Arginin	3.22	3.95	3.15	3.58	
Lysin	11.34	7.14	3.63	4.09	

The variation in these figures is due to the fact that through autolysis a more or less important change takes place, whereby various albumin substances are produced, as is shown by the above figures. The hydrolysis and analysis were performed according to the method of Weiss.

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(1b—111)

**Invertase of *Mucor Racemosus*.**

*S. Kostytschew and P. Eliasberg, Hoppe-Seyler's Ztschr. f. physiol. Chem.*, 118:233, Berlin, Jan. 25, 1922.

Of the mucor species, it is known that only *mucor racemosus* can invert cane sugar. In the course of experiments regarding the alcoholic ferment of the mucor species it resulted that only the breed *mucor racemosus* contains invertase, while *mucor racemosus* causes no inversion

at all of cane sugar. The experiments were made in such a way that with 100 c.c. yeast extract one sterile solution of cane sugar was treated with a culture of mucor racemosus + and a second with mucor racemosus —. After several days sugar tests were made according to Bertrand and polarimetric tests performed. The former culture had not formed the slightest inversion from cane sugar, while the latter culture had inverted the total amount of cane sugar and consumed much inverted sugar. With exact neutral reaction the tests gave even more definite results. Saccharose cultures may, therefore, be used with success as media for the separation of both breeds in the early stages of their development. These 2 species of fungus, which are morphologically absolutely indistinguishable, reveal very striking physiologic differences. Consequently, in the case of physiologic experiments with mucoraceae, one must observe carefully which breed serves as the subject of the experiment.

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(1b—112)

**A Well Defined Organic Catalyzer with an Optimum Hydrogen Ion Concentration.**

*Erik Widmark and Carl Axel Jepsson, Skandin. Arch. f. Physiol., 42:43, Berlin, Jan., 1922.*

Michaelis and Davidsohn have endeavored to furnish a general explanation for the effect of hydrogen ions on enzymes by assuming that the latter act only in a certain type of dissociation, i. e., either as positive or negative ions or in the form of nondissociated molecules. The activity of an enzyme would thus be an effect of the hydrogen ion concentration of the medium, since the latter primarily determines the degree of dissociation of the compound in solution.

In view of the marked similarity between the properties of enzymes and nonbiogenic catalyzers, there is inevitably a question whether, among the latter, there are some which are effective only in a given state of dissociation and ineffective in all others, consequently depending for their effectiveness upon the hydrogen ion concentration of the solvent. Experiments to prove this were made as to the dissociation of acetic acid, the constants for which had been determined by Widmark (*Acta med. scandin.*, 1920). Anilin was used as the catalyzer. The degree of catalysis would be commensurate with the dissociation of the two compounds. Only the anilin molecule was found to be effective, and that only on the undissociated molecule of acetic acid.

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(1b—113)

**The Measurement of the Sweetening Power of Artificial Saccharine Substances.**

*Richard Pauli, Biochem. Ztschr., 125:97, Berlin, Dec. 8, 1921.*

A procedure for measuring the sweetening power of saccharine substances is as follows: a solution of saccharin is prepared, which, as to its sweet taste, corresponds with a 2% solution of sugar. For this purpose 2 solutions of saccharin of markedly different concentration are prepared, one of which must be sweeter and the other should taste less sweet than the normal sugar solution of 2%, for example, one solution containing 8 mg. saccharin and the other 80 mg. A series of (Sec. 1—Page 667)

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saccharin solutions are now prepared, with strengths lying between the 2 limits and always showing the same difference of concentration; in the examples, selected solutions with the difference of 9 mg. are in the middle; this difference is designated as the stimulation standard. The observations carried out with the aid of the normal stimulation and the comparative stimulations serve the purpose of obtaining a sufficient, that is a greater number of, decisions of strength, weakness and equality. The tests were always made with a large number (207) of observers. Every pair of solutions (normal sugar solution and one saccharin solution) was tested twice with a reversal of the series. The decision must always be made after a single taste of both of the solutions so that the time error is eliminated. The tasting of the solutions occurs simultaneously by the observer at the command of the conductor of the experiment. The individual pairs of solutions are tasted in any desired order or in one that is the same for all of the participants. The sum of the individual kinds of decisions are obtained and designated numerically as weaker, stronger and equal. Both of the first figures are used in the following comparative formulas, of which the difference equals the desired comparative zone: (1)  $S_o = \frac{1}{2} (D_o + D_u + 1) - (St. i) \div N.$  (2)  $S_u = (D_o + D_u - 1) + (Sch. i) \div N.$

$S_u$  denotes the lower and  $S$ , the upper threshold; the word threshold denotes that amount of the comparative stimulation (that is, the saccharin concentration) at which the decision undergoes transition from equal to stronger ( $S_o$ ) or weaker ( $S_u$ ).  $D_u$  and  $D_o$  are the 2 end values of the comparative stimulations, the saccharin solutions of 8 and 80 mg. The factor  $i$  is equivalent to the stimulation standard;  $N$  equals the number of decisions accruing to each comparative stimulation.

In practice, the equality zone is not considered as basic, but the mean of the values  $S_u$  and  $S_o$ , to which the percentage deviation is attached. The results with this method are reliable and accurate and this procedure can be applied to the solving of all related problems, as, for example, the comparative determination of the grade of acidity of fluids.

(1b—114)

The Action of Arginase on Agmatin and Tetramethylendiguanidin. The Specificity of Ferments.

Alexander Kiesel, *Hoppe-Seyler's Ztschr. f. physiol. Chem.*, 118:285, Berlin, Jan. 25, 1922.

The chemical construction of ferments is still unknown. Thus far, albumin bodies, carbohydrates, salts and other ferments have mingled with ferment preparations. The variability of the ferments is to be explained by accidental circumstances, such as the presence of admixtures, for otherwise the number of ferments would extend ad infinitum. Perhaps it may be assumed that here the ferment is adapted to a certain grouping of atoms and that this atomic grouping must break up in the absence of inhibitory conditions. The ferment must, therefore, form a complex with the substances which have the necessary divisible atom groups, i. e., a substrate ferment. Through these admixtures, the quantitative comparison in regard to objects and inducing factors, in relation to the ferment content, is inexact, since the fermentative action is influenced by the admixtures. These admixtures may be a hindrance as regards one substance utilized for the attack, while in another case

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they may be quite without influence or even of assistance. Through them, one may also arrive at the production of ferment varieties, because they possess a varying diffusion capacity in relation to temperature, precipitating substances and desalinating substances. In order to explain these questions, experiments were performed with arginase, which was considered as an example of apparent specificity of a ferment.

Finely pulverized plant portions were used for the work. The guanidin, the substituted guanidins and the ureid were resistant to arginase. The position of creatinin is still doubtful, while for its division a ferment peculiar to itself, creatase, was assumed. Of the synthetic products, glycocyamin, guanidin acetic acid, guanidin propionic acid, e-guanidin caproic acid and  $\gamma$ -guanidin butyric acid, splitting by arginase was found only in the last. Since in all atomic complexes the guanidin grouping has the same position, the arginase must, in its different position as regards these guanidin derivatives, be influenced in activity by still other factors. Whether the decomposable grouping is an attribute of a eudogenous or to an exogenous substance should be immaterial, on the condition that there is a complex combination between substrate and ferment.

Experiments were carried out in regard to the relation of the arginase of some plant specimens to agmatin and tetramethylendiguanidin. The tests were made as follows: the plant parts were cut into small parts and finely pulverized in a mortar with quartz sand and quartz powder or infusorial earth, in the presence of toluol or toluol chloroform. The drying took place in a vacuum over sulphuric acid at  $0^{\circ}$  C. in the presence of pieces of caustic potash, in order to exclude the preventive activity of sulphuric acid fumes. The bases agmatin and tetramethylendiguanidin appeared in the form of sulphates, whereby a calculated amount of sodium carbonate was added in order to convert the sulphate into a carbonate. Control experiments were continuously carried out, without the addition of bases and with the same amount of sodium carbonate. Toluol was used as an antiseptic. The retorts were closed by Peligot tubes, with titrated sulphuric acid, against the possible ammonia content of the air. The test-tubes with ferment, with base and antiseptic and added water (about 100 c.c.) were kept in thermostates at  $37^{\circ}$  C. At the end of the experiment the ferment mixture was made slightly acid, cooked with seminormal sulphuric acid for fifteen minutes in order to put an end to the ferment activity, and thereupon the ammonia test was made by removal of the ammonia with magnesium oxid. The distillation residue was withdrawn by means of water, and the elimination of the bases accomplished by means of phosphorus tungstate, silver baryta, or picric acid.

Experiments were made with agmatin and *Aspergilis niger*, *Secale cornutum*, *Agaricus campestris* and *Vicia sativa*. The arginase of all these plant specimens failed to cause decomposition of agmatin; it remained unchanged. The same plant specimens and also with *Lupinus albus* and *Trifolium pratense*, were subjected to experiments with tetramethylendiguanidin. In these cases an action of the arginase on the tetramethylendiguanidin could be demonstrated only for the ferment of *Aspergilis niger*, although in all the tested cases the presence of arginase in the plant specimens was proved.

From the experiments it follows that, in the test with *Aspergilus* (Sec. 1—Page 669)

niger, the arginase was present in the very conditions necessary to the tetramethylendiguanidin. The arginase did not, however, find these conditions in its action on agmatin in the case of Aspergillus niger, nor in its activity, in the case of its other origin, on tetramethylendiguanidin and agmatin. By this conception as to the single existence of fermentations which are adapted only to certain atomic groupings and are greatly influenced in their activity by outside conditions, the basis of fermentation should be simplified.

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(1b—115)

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**The Fermentative Destruction of Arginin in Plants. II.**  
*Alexander Kiesel, Hoppe-Seyler's Ztschr. f. physiol. Chem., 118:267, Berlin, Jan. 25, 1922.*

In order to ascertain the extent of arginase in plants experiments were undertaken in which first the quantity of ammonia which was split off from arginin by the action of arginase and urease was determined, and then a separation of the substance formed was effected. The ergot of rye was tested, and in it there was found agmatin, a substance closely related to arginin.

The test of the fermentative arginin disintegration, carried out with the ergot of rye, demonstrates that arginase also participates in the arginin disintegration, and that under the conditions assumed the arginin is split up into urea and ornithin, but is not decarboxylized. As ferment material, 5 gm. powdered ergot of rye were used; the experiment lasted forty-six hours, and toluol served as the antiseptic. The bases present in the residues of the ammonia distillation were dissolved in warm water and precipitated with phosphorus tungstate. The arginin and ornithin fractions obtained from the precipitate were weighed, after converting into carbonate the bases contained therein, and after drying in a vacuum. The arginin fraction was found as arginin picrolonate with S.P. 221° and weighed. The ornithin as chloroplatinate was weighed and identified through the formation of ornithuric acid, S.P. 183°. From this calcium salt was now obtained. *Vicia sativa* was tested in the same manner. From the arginin fraction the arginin picrolonate was weighed and from the ornithin fraction, the chloroplatinate; ornithuric acid resulted from the latter by the use of benzoyl. In all the tests arginase could always, with certainty, be found with urease; except for ornithin and the ammonia derived from the urea, no other substances could be found. Further tests were made with ripe fruits of *Angelica silvestris* and twenty-two-day-old seed plants of *Trifolium pratense*. In both cases arginase could be found. In addition to the arginin fraction, a smaller ornithin fraction resulted. Ammonia could also be demonstrated.

These experiments, however, do not preclude the possibility that, under certain conditions and in certain plants, the arginin splitting may take place otherwise than by the formation of ornithin and urea. In such cases, agmatin, guanidin, d-aminovalerian acid and putrescin would be separated or would even be produced at the same time from arginin.

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**Emulsin.**

*R. Willstädter and W. Csanyi, Hoppe-Seyler's Ztschr. f. physiol. Chem., 117:178, Berlin, Dec. 5, 1921.*

Experiments are described dealing (1) with the yield in proportion to the plant material employed, and (2) with the activity of the preparations. For the quantitative estimation the hydrolysis of amygdalin, the decomposition of prunasin, the monoglucosid of benzaldehyde cyanhydrin, of beta-methylglucosid, of lactose and of raffinose were employed. To determine time values for emulsin effects, the authors estimated the number of minutes that would be required by 1 mg. emulsin, or plant material containing emulsin, at 30° C., to split off 50% of the theoretic amount of monose from equivalent amounts of the above-mentioned substrates under the same conditions and in each reaction with the most favorable hydrogen-ion concentrations. The pH optimum for amygdalin hydrolysis lies nearest the neutral point, for lactose and raffinose splitting it is furthest toward the acid side. The varying action of emulsin is commonly explained by assuming it to be a mixture of several enzymes. Using Willstädter's method of time value quotients it was possible to show that the emulsin reaction is due to mutually independent enzyme actions, and that emulsin preparations are varying mixtures of very numerous enzymes capable of decomposing glucosids and polyoses.

The following method of preparing emulsin was found to be the best. The almonds are converted into a dry, oil-free powder. After previous skinning they are ground in an almond mill. They are then transferred to a hydraulic press, where most of the oil is removed. They are then extracted with a threefold quantity of ether, finely ground and dried in a vacuum desiccator; 100 gm. of the dried powder are mixed in a bottle with 250 c.c. decinormal ammonia, agitated for five hours and then diluted with an equal volume of water. The ammoniated extract is separated in the centrifuge from the residues. A second and third extract are prepared and all the extracts are then combined. They contained, in the total volume of 0.5 liters, 60% of the dried substance of the almond. A large part of the albumin is treated in the customary manner with 300 c.c. decinormal or 600 c.c. seminormal acetic acid. The filtrate yields a precipitate even with 95% alcohol, consisting chiefly of albumin and gum, but it includes about 20% of the enzymes. The solution is first precipitated with a four-fold volume of alcohol and the pure white precipitate isolated by the centrifuge is then washed with absolute alcohol and ether. In acetic acid solution, and in 30% alcohol, emulsin is practically stable. The raw material (2.5-3.5 gm.) contained 60-75% of the theoretical yield. Precipitation and drying rendered a part of the protein insoluble, but the degree of purity may be easily bettered by reprecipitation. The fine powder is made into a paste with water and again precipitated with alcohol. The preparations reprecipitated in this way had a time value of 10-18, but are less stable. The preparations form clear solutions, which are light brown in great concentration.

Further tests were carried out to determine whether each case of hydrolysis produces a specific enzyme. If an enzyme is capable of splitting up several substrates with sugar or glucosids, the same time value quotients would be obtained for each with different crops or

specimens of the same original plant material, or with different materials, or on comparison of fresh or aged plant material, or on comparison of the plant material and the preparations obtained from it, or with preparations of different degree of purity, or with different species. So far no proofs have been obtained of such a correspondence in time values. It remains to investigate how much the time conditions differ in the decomposition of the mutually related phenolglucosids such as salicin, helicin, coniferin and arbutin. Such an investigation will show the degree of specificity of the glucosid-splitting enzymes of plant seeds. All emulsin reactions examined up to the present involve enzyme actions which are mutually independent and take place, at times, under varying conditions.

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(1b—117)

**Emulsin.**

*B. Helferich, Hoppe-Seyler's Ztschr. f. physiol. Chem., 117:159, Berlin, Dec. 5, 1921.*

Emulsin is able to split up a large number of glucosids of the beta-series into their constituents, from which it is concluded that it contains a specific ferment necessary for this splitting, viz., beta-glucosidase. The latter may be a mixture of different ferments. The authors describe experiments to determine the activity of beta-glucosidase, then illustrate the preparation of the most active obtainable ferment, and describe some of the properties of the beta-glucosidase so obtained which could be observed by exact measurements. For determining the activity of beta-glucosidase the polarimetrically observed decomposition of salicin was employed. In order to maintain a definite hydrogen-ion concentration, sodium acetate and acetic acid were employed in accordance with the method of Michaelis. The rotation was observed in a 2 decimeter tube. For interrupting the experiment, solid powdered potassium carbonate (0.2 gm. to 5 c.c. glucosid solution) was used. The splitting up of salicin by beta-glucosidase takes the form of a monomolecular reaction. The equation employed for the calculation was:  $K = \text{reciprocal of } t \text{ multiplied by the logarithm of } [(A - E) \div (a_1 - E)]$ ;  $t$  is the duration of time during which the ferment acts,  $A$  the initial rotation,  $E$  the final rotation of the glucosid solution up to complete splitting, and  $a_1$  the rotation of the solution after the interruption of the experiment at the time  $t$ . The rotation times are not to be considered in this.  $K$  was generally multiplied by 10 in order to obtain more convenient figures.

The emulsin was prepared from plum-stones, which were comminuted, pressed, extracted with water, filtered and precipitated with alcohol. From the dilute solution an active preparation was always obtained. By means of dialysis the emulsin so obtained could be purified considerably further. The preparations of emulsin were white powders. They were easily soluble in water. Boiling with alcohol reduced the activity, but keeping in absolute alcohol did not affect the activity. Digestion with pancreatin and subsequent dialysis produced an emulsin free from albumin, which gave no biuret reaction, and whose activity was less, although still strong.

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Notes on Cholesterol.

A. Windaus, *Hoppe-Seyler's Ztschr. f. physiol. Chem.*, 117:146, Berlin, Dec. 5, 1921.

Several experiments conducted during a study of the decomposition of cholesterol are communicated. From cholesterol the diketone cholestan may be prepared in various ways. It yields a ketodicarbonic acid,  $C_{27}H_{44}O_5$ . The reduction of the carbonyl group in the acid,  $C_{27}H_{44}O_5$ , was effected by L. Wolff's method, and the semicarbazone of the ketodicarbonic acid was decomposed with sodium ethylate. Ketodicarbonic acid,  $C_{27}H_{44}O_5$ , on thermic decomposition or in high vacuum distillation, yields a cyclic diketone,  $C_{26}H_{42}O_2$ , in which the acid splits off one molecule water and one molecule carbon dioxid. The neutral constituent crystallizes and melts at 148° C. The dioxid prepared in alcoholic solution with hydroxylamin hydrochlorid and sodium acetate melts, after recrystallization from alcohol, at 191° C. Cholesterol is derivable from cholestan. Of characteristic groups cholesterol contains a hydroxyl group and a double compound of the carbon bodies 6 and 7. Cholic acid possesses a carboxyl group which stands in an aliphatic sidechain, and 3 hydroxyl groups whose position is not yet fully determined. The oxidation of cholic acid leads to dehydrocholalic acid,  $C_{24}H_{34}O_5$  and thence to bilanic acid and isobilanic acid, which represent structural isomerids. As cholesterol, on being treated with perbenzoic acid, gains one atom of oxygen, alpha-cholesterol oxid is produced, and also small amounts of the isomeric beta-cholesterol oxid. On treatment with water the former is converted into alpha-cholestane-triol. Mauthner and Suida prepared hydrocarbons of the formula  $C_{27}H_{44}$  from cholesterol, with anhydrous copper sulphate. Tschugaeff and Fomin obtained these bodies with xanthogenic acid ester from cholesterol, which they named cholestylene. During the preparation it was found that the cholestylene obtained with copper sulphate takes up 2 molecules hydrogen and, therefore, possesses 2 double combinations, like Tschugaeff's cholestylene. Reduction yielded partly cholestan and also a mixture of 2 isomeric saturated hydrocarbons which were identified as cholestan and pseudocholestan.

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The Determination of Small Amounts of Nitrogen after Kjeldahl.

J. K. Parnes and Richard Wagner, *Biochem. Ztschr.*, 125:253, Berlin, Dec. 18, 1921.

For the so-called microdetermination of nitrogen Pregel's method was so modified as to avoid the liability to fracture of the distillation adapter, and the danger of contaminating the fine glass by strong alkali. The distillation flask and the adapter were made in one piece and received the addition of several appliances for filling and emptying the apparatus. The apparatus is cheaper than Pregel's, as it is not polished and is not exposed to any injuries. It permits of quick determinations following rapidly on each other. The exact arrangement is illustrated by a diagram. The apparatus is also suitable for serial estimations and for this purpose a glass frame is employed which is intended for 6 simultaneous incinerations. The eprouvettes are charged with the substance to be incinerated, as, for instance, with urine; then sulphuric

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acid, potassium sulphate and copper sulphate are added, each receives 3 glass beads, and they are then placed in an oblique position in the frame and heated over Bunsen burners.

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**The Resolution of Hydroxyaspartic Acids into Optically Active Forms.**

*H. D. Dakin, J. Biol. Chem., 50:403, Feb., 1922.*

In a previous paper Dakin described the synthesis and separation of two inactive forms of hydroxyaspartic acid. The inactive form, more soluble in water, gave mesotartaric acid on treatment with nitrous acid and was designated as the anti compound, while the less soluble form gave racemic acid under similar conditions and was named the para compound. Each of these inactive acids contains 2 dissimilar asymmetric carbon atoms and should be resolvable into active components, giving a total of 4 active and 2 inactive forms. The resolution of the anti acid was readily effected by means of such alkaloids as quinin, brucin and strychnin. The para acid could not be resolved by this method, although its finely crystalline alkaloid salts were subjected by Dakin to exhaustive fractional crystallization. It appears that the alkaloidal salts of the para acid are partially racemic compounds of the type described by Ladenburg. On turning to alternative biological methods for the resolution of the para acid it was found that no resolution could be effected by growing penicillium glaucum in solutions of the sodium salt while some rather inclusive evidence was secured of a slight resolution by fermenting yeast used according to Ehrlich's method. The small amount of dextrorotatory acid thus obtained gave dextrotartaric acid on treatment with nitrous acid. Since the Walden inversion rarely occurs with nitrous acid it is probable that d-hydroxyaspartic acid and d-tartaric acids are similarly constituted, and the same would be true of the levo forms. Both active forms of anti-hydroxyaspartic acid give inactive mesotartaric acid on treatment with nitrous acid so that their relative configuration remains undecided. On heating either of the active anti acids with water at 125°, partial conversion into the para acid was effected, but the latter was invariably optically inactive.

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**A Coupled Nucleic Acid from the Pancreas. II.**

*Einar Hammarsten and Erik Jorpes, Hoppe-Seyler's Ztschr. f. physiol. Chem., 118:224, Berlin, Jan. 25, 1922.*

In the alkali hydrolysis of a nucleic acid obtained from the pancreas, the sodium salt of guanylic acid and a residue containing pentose could be split off, according to Hammarsten. Feulgen obtained the sodium salt of guanylic acid by the alkali hydrolysis of the guanylic nucleic acid isolated by him from pancreas. This seems not to be identical with that obtained by Hammarsten, since after the complete removal of the freed guanylic acid there remains still a considerable content of pentose and no purin bases other than adenin. Since this is of importance for understanding the mode of combination of guanylic acid in pancreas, experiments relating thereto were undertaken.

The calcium-sodium salt of the collective nucleic acids was obtained  
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from the pancreas according to the method described in the Biochem. Ztschr., 109:141; after hydrolysis in alkaline solution, the sodium salt of guanylic acid was centrifuged off and treated with sulphuric acid; the guanin was precipitated with ammonia and thereby identified as the sodium salt of guanylic acid. The filtrate and wash water gave good reactions for pentose. From the guanylic acid, the brucin salts were also obtained. Analysis showed that on alkali hydrolysis the nucleic acid obtained by Hammarsten from pancreas splits into guanylic acid and a substance which contains pentose and adenin as the sole purin base. The appearance of hydrolysis upon warming with alkali the collective nucleic acids which were being investigated (whereby acid combinations become free), and the pentose content even after removal of the guanylic acid, make a similarity to yeast nucleic acid probable. Since, however, a small quantity of hexose was shown in the collective nucleic acids, the presence of thymo nucleis acid, which also should be present in pancreas, may be concluded.

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**The Supposed Formation of Hydrogen Peroxid in Carbon Dioxid Assimilation.**

*Hans Molisch, Biochem. Ztschr., 125:257, Berlin, Dec. 18, 1921.*

Kleinstück is of opinion that the assimilation of carbon dioxid leads to the formation of hydrogen peroxid but this has not been confirmed so far by any plant physiologist. The formation of ozone was also claimed without any proof being obtainable, Kleinstück's experiment was carried out on Elodea. He poured Seltzer water over these and then placed them in bright sunlight until oxygen was generated. He found that if a few centimeters are acidified and potassium iodid starch paste added an immediate blue coloration is obtained, which is characteristic for hydrogen peroxid. He held that by means of adequate and stronger assimilation the presence of hydrogen peroxid may also be confirmed, with the chromic acid-ether reaction. In control experiments undertaken in the Physiologic Institute at Vienna and in the Biologic Institute at Linz, which were conducted not only with Elodea but also with Potamogeton prelongus, Chara sp. and Myriophyllum verticillatum, hydrogen peroxid could not be detected in any case. It is probable that Kleinstück's observation was due to iron which is found frequently in plants and gives the same blue color with potassium iodid starch paste as does hydrogen peroxid.

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**Synthesis and Properties of Tetramethylendiguanidin.**

*Alexander Kiesel, Hoppe-Seyler's Ztschr. f. physiol. Chem., 118:277, Berlin, Jan. 25, 1922.*

In the experiment for producing agmatin with arginase, cyanamid was introduced in portions and in excess. In addition to agmatin, another base was produced, which appeared as tetramethylendiguanidin and then as a homologue of pentamethylendiguanidin. About 34% of the putrescin used was obtained as tetramethylendiguanidin sulphate.

As the guanidin group forms no nitrate with nitric acid, by Van Slyke's method, it was ascertained by experiment that there are no  
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free NH<sub>2</sub> groups contained in tetramethylendiguanidin, so that both groups stand at the end of the chain. Thus far, only one natural diguanidin is known, i. e., the vitiatin from meat extract. It is possible that these diguanidins have a certain physiologic rôle. On the basis of the sulphate some salts were produced, namely: carbonate, sulphate, chlorid, picrate, picrolonate, chloraurate and chlorplatinate of tetramethylendiguanidin. The tetramethylendiguanidin could be precipitated quantitatively by the silver baryta process, in the presence of an excess of baryta. Likewise, it may be precipitated in an approximately quantitative manner by tungstate of phosphorus in acid solutions.

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**Distribution of Urease among Plants.**

*A. Kiesel and Troitzki, Hoppe-Seyler's Ztschr. f. physiol. Chem., 118:247, Berlin, Jan. 25, 1922.*

Urease has, up to the present time, been found only in plants and produces a ferment. Urea is apparently present in plants as an intermediary, in animals as a final product of metabolism. Experiments were made in order to determine how widely urease is distributed in the plant kingdom. There were tested with negative result: inner bulb squama of Allium cepa, roots of Beta vulgaris and Daucus carota, resting and active tubers and the shoots from these nodules of Solanum tuberosum, leaves and stems of Pelargonium zonale. Everywhere the quantity of ammonia was too small to make it possible to speak of any urease action. From the tests it appeared that the drying of the material diminished the activity of the urease. Previous autolysis in a damp room strongly reduces the action of fermentation. A decline of fermentation activity could be shown for the state of ripeness of the fruits of Angelica silvestris. Prolonged preservation also interferes with the urease. Since, by keeping the seeds in a vacuum, the action of the urease remains the same, it would appear that the water content of the material influences the efficacy. From the experiments on the influence of light and the influence of better nourishment on urease formation, no general conclusion could be drawn, probably individual and age differences played a part. In the experiments made to determine the distribution of urease in different organs of the plants, a larger amount of urease was found in the leaves than in the stems and roots; this was true for green plants as well as for dry plants. In no seed does the urease action seem increased. The experiments were carried out on Aspergillus niger, Vicia sativa and Phaseolus vulgaris, as also on Pisum sativum, Helianthus annuus and Angelica silvestris.

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**Hemolytic and Water Fevers.**

*W. J. Penfold and D. G. Robertson, M. J. Australia, 1:29, Sydney, Jan. 14, 1922.*

In contradistinction to the conclusions of Hort and Penfold, Yama-kami found that the intravenous injection of suitable quantities of dis-  
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tilled water gives a typical fever, which he is satisfied is due to hemolysis. He found these quantities to be equivalent to  $1/186 - 1/54$  of the body weight. This challenge to the work of one of the writers led them to repeat this portion of Yamakami's work. The experiments were conducted on 12 English and 6 wild Australian rabbits. The glassware used was scrupulously cleaned by treating with a concentrated sulphuric acid-potassium bichromate mixture. It was then rinsed with ordinary distilled water, followed by sterile freshly distilled water and then autoclaved. The rubber corks were boiled in a soda solution, mechanically cleaned, boiled in freshly distilled sterile water and autoclaved. The still used consisted of a round-bottomed 2-liter hard-glass boiling flask fitted with a 3-holed stopper protected by tinfoil. Through one hole was passed a glass safety-tube of 0.6 cm. bore going to the bottom of the flask and surrounded above by a cotton wool band which fixed an enveloping glass shield (a 5 cm. by 1.25 cm. test-tube). Through the second hole was passed a glass feed-tube drawn out to a capillary point and extending about 3.75 cm. below the stopper. To the outside end of this tube was wired a small piece of India-rubber pressure-tubing, protected at its end by a glass shield, which shield was held in position by a cotton wool band. The third hole was pierced by a glass tube connected with an ordinary spray-trap, such as is used in Kjeldahl's ammonia-distillation apparatus. This was joined by a rubber stopper to an upright condenser. The rubber stopper was protected by tinfoil. The delivery tube of the condenser was fitted with a glass hood, so that sterile water could be received. The injections were made into the marginal veins of the ear. Twelve experiments were made with varying amounts of water. It was found that the temperatures of the English rabbits ranged between 39.5° C. and 38.7°, and those of the Australians between 39.2° and 38.7°. Variations of as much as 0.5° were observed in the thermometric readings of individual rabbits in the course of a day. It was apparent that distilled water is unable to produce fever on intravenous injection, although administered in the quantities recommended by Yamakami. The writers believe that his distilled water was not prepared with sufficient care and that his rabbits suffered from some slight infection. It was shown by Hort and Penfold that distilled water sensitizes the body to bacterial intoxication, and it may be that rabbits which have latent infections and normal temperatures may give a fever on the intravenous injection of even pure water.

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**The Effects of Various Foods, Food Factors and Chemical Agents upon the Resistance of Animals to Acetonitril.**

*Masataro Miura, J. Lab. & Clin. Med., 7:267, Feb., 1922.*

Miura reviews the literature regarding demonstrations of the resistance of animals to different poisons when fed on certain kinds of food. He believes that, since an insufficient diet manifests itself in altered metabolism, the influence of controlled intake, both qualitative and quantitative, is of prime importance in making investigations on the action of poisons in the animal body. On the theory that acetonitril is a poison in the animal body and acts as a delicate test for changes in metabolism, he used experimentally, as a basal diet, a food mixture composed of standardized synthetic foods, qualitatively and calorifically

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sufficient. Studies were made of the variations in resistance of mice to acetonitril when given different diets. Accompanying tables give the effect of lack of vitamin, of underfeeding, rate of growth, diets low in protein, high in fats, kind of fat, various animal tissues, mineral elements, kind of protein, and effect of oat-starch.

The results indicate that no alteration in the resistance to acetonitril was secured except in cases of underfeeding, of feeding with iodin as the sole mineral, and in feeding with oat-starch. Consequently this led to the deduction that as the susceptibility of mice to poisoning with acetonitril is not readily affected by starches, in dietary composition within wide limits of quantity and quality, it may serve to emphasize the safety of the organism in responding to alterations of the diet.

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**The Effect of Alcohol on Sport Activity.**

*Herbert Herxheimer, Münch. med. Wchnschr., 69:143, Feb. 3, 1922.*

Ergographic records show, in general, that the accomplishment of work is increased shortly after the ingestion of alcohol, as a result of increased will impulse and not as a result of greater strength during muscular contraction. It is known that sport activity must be measured in other ways than by merely ergographic methods. There is a limitation of the action of a particular group of muscles in ergographic determinations performed in the laboratory, but the muscular activity is more generalized in exercise. The nervous elements also play a prominent part in exercise, and can hardly be separated from the muscular effort. Experiments were undertaken to determine whether or not alcohol really had a favorable influence on exercise and muscular activity. Sports had to be chosen which lasted for a short time only, in which the examination could be made early enough to demonstrate the effect of alcohol, and which would end before the fatigue factor came into play. A sprint for 100 meters was chosen as the form of exercise, as this represents a concentrated type which lasts twelve or thirteen seconds and does not require very much effort at coöordination.

The experiments of the author were carried out with consideration of all outer factors such as the nature of the running-path, wind, time of day and weather. The same persons always ran together. The muscular accomplishment of all was nearly alike. The same persons ran together 3 or 4 times for 100 meters, so that the comparative accomplishment could be determined. Seven cubic centimeters of 96% alcohol were given in aqueous solution. Only one-half of the subjects took this alcohol, while the other half did not, but were made to believe that they had by means of drinks which produced the same stimulating sensation in the mouth.

The experiments were performed with running and swimming for 100 meters, under the precautions mentioned. The results showed that the ingestion of even small quantities of alcohol just before the test produced a reduction in the powers of the subject of the experiment. This shows the error of the widespread belief that small doses of alcohol are useful just before exertion.

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**Effect of Ethyl Alcohol on Tadpoles.**

*S. O. Mast and Y. Ibara, Am. J. Physiol., 59:394., Feb. 1, 1922.*

In the authors' experiments, a large number of frogs' eggs all deposited by one female was brought to the laboratory and two days later there were numerous tadpoles. These were taken at random and put into cultures in 6 battery jars. Two of the small jars contained each 700 c.c. of 0.66% alcohol, one with plants (*elodea* and *nitella*) the other without. Two contained 0.33% alcohol, one 700 c.c. with plants, the other 350 c.c. without plants. The remaining small jar contained 350 c.c. tap-water without plants, and the large jar contained 1000 c.c. tap-water with plants. No food was added to any of the cultures except the plants and alcohol as indicated. The jars were all kept side by side in strong indirect sunlight and the solution in each one was renewed every morning. Whenever the tadpoles were put into a fresh solution of alcohol they became extremely active and swam about violently for a few minutes. The tabulated results show that the tadpoles which were subjected to alcohol lived longer than those which were not, but those in the weaker solutions lived longer than those in the stronger. This was especially marked in the solutions with no plants. After the tadpoles had been in the solutions a few weeks it was very evident that those in the alcohol, especially the 0.66%, were larger than those in water. The author states that it is not clear how these effects are produced.

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**Gas Metabolism of Curarized Frogs. I. The CO<sub>2</sub> Output.**

*Hans Rosencrantz, Pflüger's Arch. f. d. ges. Physiol., 193:39, Berlin, Dec. 8, 1921.*

It is remarkable how rapidly the blood of a curarized frog becomes venous. Immediately following the onset of paralysis the bright red color disappears. This points to a marked decrease in the oxygen content of the blood consequent upon respiratory paralysis. It would be of great interest to determine to what extent the exchange of gases persists in the frog in the course of curare poisoning. To begin with one has to count on the possibility of total stoppage of oxygen intake, the animal therefore leading an anaerobic existence. According to Pflüger's observations, a normal anaerobic frog dies in about eighteen hours. But curarized frogs survive their paralysis for three days without apparent harm. They must therefore be considered as existing in entirely different conditions of life from those of a normally breathing frog. One can readily imagine that following curarization there is a marked diminution in metabolism as a result of the paralysis, thus rendering duration of life greater even under anaerobic conditions than in a normal animal; on the other hand there exists the possibility of a diminished CO<sub>2</sub> output in the curarized as compared to the normal frog, and that an accumulation of this gas in the blood may exert an anesthetic action on the animal, resulting in this manner in a diminution of the metabolic processes.

Rosencrantz attempted to solve the problem experimentally. His results are the following: The normal frog's average hourly output of CO<sub>2</sub> varies from 22.02 to 59.44 c.c., with a mean of 41.75 c.c. per kg. of body weight. In the curarized animal the metabolism is reduced

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to about one-half (14.56 to 36.16, with a mean of 22.52 c.c.). The production of CO<sub>2</sub> is greatest at the beginning of paralysis, then begins to decline and remains constant after the fifth hour. Exsanguinated curarized frogs have a CO<sub>2</sub> output equal to about one-third that of the normal and to about one-half that of the curarized frog. The skin cells are only very moderately participating in the CO<sub>2</sub> elimination. In the exsanguinated frog the CO<sub>2</sub> output is greater the smaller the experimental animal, i. e., the greater the relative body surface.

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**Studies on Stimulation of the Respiration: The Action of Respiratory Stimulants upon the Respiration When Depressed by Increased Intracranial Pressure, with Special Reference to Sodium Cyanid.**

*A. S. Loevenhart, J. Y. Malone and H. G. Martin, J. Pharmacal. & Exper. Ther., 19:13, Feb., 1922.*

The experiments have fallen into 2 classes: those in which a constant relation was maintained automatically between the blood pressure and intracranial pressure, and those in which the intracranial pressure was held at a constant level and did not alter with changes in the blood pressure. Under the first class, studies were made of the effect of various drugs on the respiration when it was depressed by a constant grade of medullary anemia, and under the second class, studies were made of the effect of various respiratory stimulants when the respiration was depressed by a constant grade of intracranial pressure. It was found that sodium cyanid is the most reliable stimulant to the respiration when depressed by intracranial pressure. It exercises its stimulating action on the respiratory center directly, and acts independently of any change which it produces in the circulation. The changes in the blood pressure following therapeutic doses were insignificant. The effects lasted only a very brief period, usually not over one minute, but occasionally stimulation lasted for as long as thirty minutes. By giving cyanid continuously at the proper rate, continuous stimulation of the respiration may be maintained for hours. Sodium cyanid must be administered intravenously. The dosage for stimulation of the respiration in the dog by single rapid injections is 1-3 mg. The dosage for continuous injection to maintain stimulation already established is approximately 0.25 mg. (0.5 c.c. of a 0.01 N solution) per minute.

Strychnin sulphate given intravenously stimulated the respiration in about 25 to 50% of the experiments, but stimulation was not so prompt or reliable as in the case of sodium cyanid, although the stimulation following a single dose lasted much longer. Atropin sulphate caused slight stimulation of the respiration, in certain animals, but in most animals no stimulation was observed. The removal of vagal tone by the atropin caused a marked increase in the pulse-rate and a rise of blood pressure. This had a beneficial effect on the respiration, but only for a very brief period, because the circulation collapsed with striking suddenness. In some cases, brief but definite stimulation of the respiration by caffeine citrate was noted. In spite of this stimulation, its effect seemed to be harmful rather than beneficial, the harmful effect being attributable to changes in the circulation, although the cause of the deleterious action was not investigated. In most cases lactic acid exerted no stimulating action.

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**The Action of Dimethyltellurium Dihaloids.**

*Douglas V. Cow and W. E. Dixon, J. Physiol., 56:42, London, Feb. 14, 1922.*

To determine the relations between molecular structure and physiologic action, the authors administered to cats, dogs and rabbits 2 isomeric dimethyltellurium dichlorids, referred to as the  $\alpha$  compound and the  $\beta$  compound. The immediate effect of the intravenous injection of 5 mg. of the  $\beta$  compound into the circulation of the anesthetized cat or dog, is a rise in blood pressure with increased frequency and depth of respiration. This effect lasts about thirty seconds, then the blood pressure rapidly falls to normal. This is followed by a secondary rise usually more marked and more prolonged than the first. After each succeeding injection the effects become less pronounced. The injection of 5 mg. of the  $\alpha$  compound into a cat causes the heart to stop beating instantly and the blood-pressure to fall to zero. But after about thirty seconds the heart beats again and the blood pressure exceeds the original, normal height. Respiration is little influenced by the  $\alpha$  compound nor does the heart appear to be permanently damaged even if large doses of the  $\alpha$  compound are administered. In explaining the vascular and respiratory effects following injection of the  $\beta$  compound the authors state that if the spinal cord of an animal is severed below the medulla the primary rise of blood pressure is almost entirely absent. Similarly if the central nervous system of an animal is completely paralyzed by nicotin the  $\beta$  compound fails to produce any initial rise of pressure. This augmented pressure is mainly due to vasoconstriction. The vasoconstriction is not peripheral for the reason that perfusion experiments on isolated organs show that the  $\beta$  compound never constricts vessels but rather tends to increase the outflow from the veins. The secondary rise in blood pressure occurs in decerebrate animals and in those in which the whole central nervous system has been paralyzed by apocodein or nicotin. This effect is mainly due to vasoconstriction of peripheral origin, but is not due to the direct action of the drug. If the suprarenal glands of an animal are ligatured and excised, the injection of  $\beta$  compound causes no secondary rise of blood pressure, suggesting that the  $\beta$  haloid may act on the suprarenal glands and that the rise of blood pressure may be due to the liberation of adrenalin. Section of the 2 splanchnic nerves in the cat did not materially influence this secondary pressor action of the drug, although it usually cut out almost completely the primary pressor action by separating the medulla from the splanchnic area. The  $\beta$  haloid does not excite any part of the nervous system directly, except the medulla. The  $\beta$  haloid exerts an adrenalin action on the heart in the second phase, the  $\alpha$  compound acts on the contractile tissue of the heart directly and causes standstill. The  $\alpha$  haloids cause plain muscle throughout the body to contract. The  $\beta$  compounds have no peripheral action on plain muscle of note. Large doses of the  $\beta$  haloid paralyze nerve structures in the following order: (1) sympathetic ganglion cells, (2) other autonomic ganglion cells, (3) medulla and motor nerve endings.

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**Centrifuging Experiments with Etherized Spirogyra.**

*Friedl Weber, Biochem. Ztschr., 126:21, Berlin, Dec. 27, 1921.*

Centrifugation was employed in order to find out the changes of viscosity in the living cytoplasm. Etherized spirogyra were used for the experiments, which were carried out in May and September. The algae possessed a single chromatophor and showed a groove on the partition wall. Equal quantities of spirogyra were put into centrifuge tubes. Then 2 controls, one without ether, the other in etherized tap-water, were centrifuged. Samples of these controls were microscopically examined immediately after centrifuging. By using medium magnification in counting the cells, the percentage of cells whose chloroplast was dislocated, could easily be determined. Average values were taken. The experimental records show, that according to the concentration of the ether by centrifugal force, the chloroplastic band of etherized spirogyra is more easy or more difficult to dislocate than the bands of controls which were kept in ether-free tapwater. At a weak ether concentration up to 2.5 volumes per cent. and a duration of action of one to two hours, the dislocation was easier; at higher ether concentrations of approximately 3 volumes per cent. and above, it was more difficult in a smaller number of organisms than in the control experiment. At an ether concentration of 2.5-3 volumes per cent. it depends upon the duration of the action. The dislocation-furthering effect of weaker doses, as well as the dislocating-inhibiting effect of stronger doses, is reversible, i.e., it may be made to disappear by washing the spirogyra in water for several hours.

This change in the susceptibility to dislocation is most likely due to the change of the viscosity in the living cytoplasm. This viscosity is decreased by small doses of ether and increased by large doses. Both effects of the narcotic are reversible. The results of these experiments are in accordance with the findings of Heilbronn, in higher plants and sea-urchin eggs. It seems that in the function of the plasma disturbance, in spirogyra, the stimulation phase of anesthesia is dealt with, while the effects in the cell division are the expression of the paralyzing phase of the anesthetic.

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**The Erythropoietic Action of Germanium Dioxid.**

*Frederick S. Hammett, Joseph E. Nowrey, and John H. Müller, J. Exper. Med., 35:173, Feb., 1922.*

Injections were made of a solution of germanium oxid into rats, which responded to the injections by a marked and sustained rise of from 1 to 5 million erythrocytes. Corresponding changes in the bone-marrow were noted. Germanium dioxid is nontoxic and noncorrosive, and is further of interest on account of its relation to arsenic, germanium coming next to arsenic in the periodic system.

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**Erythropoietic Action, Cumulative Effect and Elimination of Germanium Dioxid.**

*John Hughes Müller and Miriam Steward Iszard, Am. J. M. Sc., 163:364, March, 1922.*

This investigation was undertaken to determine: (1) the erythro-  
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poietic action of germanium oxid on animals other than the albino rat; (2) the toxic effect of large doses; (3) the cumulative effect of the compound in the system; and (4) the mode of elimination of the compound from the system. The authors conclude that: (1) Germanium dioxid has a decided erythropoietic action in the guinea-pig, rabbit, dog, and man, and that this action exerts a certain periodicity as shown in all of the erythrocyte curves obtained. (2) Relatively large doses of germanium dioxid are distinctly toxic, and from the results obtained it can be roughly calculated that the lethal dose is about 586 mgm. of germanium dioxid per kilo of body weight. (3) This toxic action is not explainable on the basis of the accumulation of the compound in the system, but is possibly due to an overstimulation of the blood-forming organs. (4) The quantitative method devised by the authors for the determination of germanium dioxid in animal tissues and excreta, both in the presence and in the absence of arsenic, is an accurate method, and permits the detection of as small a quantity of germanium dioxid as 0.0002 gm. (5) Germanium dioxid does not accumulate, but is eliminated through the kidneys and alimentary tract. The overdose being rapidly eliminated, chiefly through the agency of the kidneys, elimination by way of the alimentary tract is small.

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**The Action of Drugs on the Output of Epinephrin from the Adrenals. VIII. Morphin.**

*G. N. Stewart and J. M. Rogoff, J. Pharmacol. & Exper. Ther., 19:59, Feb., 1922.*

Morphin, administered subcutaneously or intravenously, causes in cats an increase in the rate of output of epinephrin from the adrenals. As much as 10 times the initial rate has been observed. The animals were anesthetized with ether (in one experiment with urethan) before the morphin was administered, and therefore it is not known what increase may be caused in the absence of these anesthetics, which do not themselves appear to increase the output. The symptoms produced by morphin in nonanesthetized cats cannot be due, in any important measure to an increased output of epinephrin, since they are all obtained, and apparently in undiminished intensity, in cats after removal of one adrenal and the chief part of the other, and denervation of the remaining fragment. In dogs, either no increase in the output of epinephrin or a very slight one was caused by morphin. This difference in the action of the drug in the two animals is as marked as the other pharmacological differences.

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**The Influence of Morphin on Normal Cats and on Cats Deprived of the Greater Part of the Adrenals, with Special Reference to Body Temperature, Pulse and Respiratory Frequency and Blood Sugar Content.**

*G. N. Stewart and J. M. Rogoff, J. Pharmacol. & Exper. Ther., 19:97, Feb., 1922.*

The marked hyperthermia caused by morphin in cats (the rectal temperature increasing as much as 4° C.) has been studied in connection with the development of the general symptoms, the changes in the (Sec. 1—Page 683)

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pulse and respiratory frequency, and the sugar content of the blood. It was observed that there is no close association between the hypothermia and the hyperglycemia, or even the degree of muscular activity. The hyperthermia and the general symptoms developed in the same way, and reach the same intensity in cats from which the greater portion of the adrenal tissue has been removed and the remaining fragment denervated, as in normal cats. No foundation was found for the statement that adrenalectomized rats succumb to a very much smaller dose of morphin than normal rats.

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**The Influence of Salvarsan upon the Serum of Animals and upon the Formed Elements of the Blood in Vitro.**

*J. L. Kritschewsky, Biochem. Ztschr., 126:11, Berlin, Dec. 27, 1921.*

The symptoms accompanying the death of animals killed by salvarsan administration, as well as the results of autopsy, are the same as in anaphylactic shock. In both cases, the shock results from changes in the degree of the dispersion of the colloids of the organism. The present experiments show that salvarsan has the capacity to change the degree of dispersion of colloids; the effects of the salvarsan in vitro on the serum of the animals and the formed elements of the blood were examined. In the first place, the precipitating properties of the salvarsan were established. One c.c. of the salvarsan dilution in 0.85% saline solution were put into a test-tube to which immediately 0.1 c.c. of horse serum were added with a Pasteur pipe. The result was considered positive or negative according to the appearance or the absence of a precipitation-ring in the zone of contract between the two liquids. The experiments show that salvarsan has the property to reduce the grade of dispersion of colloids in an alkaline or acid solution; 0.001 gm. salvarsan causes precipitation of the serum. To a certain degree the precipitate reaction cannot be recognized in the presence of a salvarsan excess. The resulting precipitate is, within certain limits, made soluble by the salvarsan excess. The salvarsan is capable of agglutinating different types of erythrocytes. Acid and alkaline salvarsan solutions are used for the experiment to 1 c.c. salvarsan solution diluted in 0.85% saline solution. 0.25% suspension of erythrocytes, which was washed in a physiological salt solution, were added. The mixture was thoroughly shaken, put in 37° for an hour and then the precipitate was determined. The experiments show that the agglutinating properties of salvarsan are very high. In an alkaline solution, the agglutination takes place in the presence of 0.0002 gm. in acid solution of 0.00001 gm. It also was shown that the salvarsan was absorbed by the serum and the erythrocytes and that the constituent of the substance remaining in solution is either completely unable to change the grade of dispersion or is at least only slightly effective. Moreover, there was proof of a hemolytic action of the salvarsan, although there are differences in the blood corpuscles of different species. The agglutinating action of the salvarsan, however, in alkaline as well as in acid solution, is greater than the hemolytic action. In the hemolysis experiment, the mixture of 1 c.c. salvarsan solution plus 0.5% erythrocyte suspension was kept in 37° for an hour. The mixture was shaken up several times and

finally centrifuged. The hemolytic action of the salvarsan, as well as the precipitating and agglutinating properties of salvarsan, may be neutralized by addition of serum, although the action of salvarsan is, in part, selective; for instance, serum, in certain quantities, showed neutralizing action upon the hemolytic action of salvarsan in the case of the red blood corpuscles of sheep, chicken and man, while it was ineffective in the case of the erythrocytes of the horse.

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**The Pharmacology of Selenium and Tellurium.**

*Georg Joachimoglu and W. Hirose, Biochem. Ztschr., 125:1, 5, Berlin, Dec. 8, 1921.*

It has been possible to show that bacteria are comparatively sensitive to tellurites, tellurates, selenites and selenates, but mold fungi are hardly influenced by them. The conclusion was drawn that these salts could be used therapeutically. Tests were made in cases of colon infection of the bladder and on bacillus-carriers. The following experiments were conducted to determine how diphtheria bacilli behave when the tellurium concentration is increased and also whether there is any difference between the tellurites and tellurates in this respect, and how the corresponding selenium combinations behave: The solutions of sodium combinations of the tellurites and telluric acid and of the selenites and selenic acid were diluted with glucose bouillon; 3 drops of a suspension of diphtheria bacilli were put into each of the corresponding dilutions of the salts with glucose and incubated for twenty-four hours. The adduced tables showed that the diphtheria bacilli are killed only by high tellurium and selenium concentrations respectively: in tellurite dilutions of 1:420, in tellurate dilutions of 1:125; in selenite solutions of 1:1460 and in selenate dilutions of 1:666. The bacilli of the typhoid-colon group are killed by a 400 times smaller tellurium concentration. The selenites and tellurites are more effective than the selenates and tellurates. The high power of resistance of diphtheria bacilli is associated with their high power of reduction; they reduce the oxygen combinations to metallic selenium and tellurium respectively and these are not toxic.

As a sequel to investigations upon the toxicity of the arsenious and arsenic acids on the isolated frog's heart, in which a great difference was noted between the two, analogous experiments were made with tellurous and telluric acids and with selenious and selenic acids; the sodium salts of these acids and these with varying amounts of Ringer's solution were used. The pH of the applied solutions usually amounted to 7.2-7.4 and the concentrated tellurite solution showed a somewhat alkaline reaction—pH 7.6-8.0 Land frogs were used with a weight of 40-50 gm. and the isolated heart worked with a Straub cannula. The tellurite concentrations were 1:80,000 and the tellurate concentrations, 1:100-1:10000. With the tellurite, arrest of the heart action was observed with a tellurium concentration of 1:40,000, but with tellurate the heart continued to act even after twenty hours with a tellurium concentration of 1:200. With selenite, arrest of the heart action occurred with a selenium concentration of 1:300,000 after four and a half hours, but with selenate, the same effect occurred with a selenium concentration of 1:3000. Accordingly, the tellurite is at least 200 times more toxic with reference to the heart than the selenate.

The effect of these combinations upon the blood pressure in warm blooded animals was also tested. Rabbits were anesthetized with urethan, a glass cannula was introduced into the trachea for the registration of respiration and this was connected in the usual way with a Marey's tambour; a cannula was introduced into the carotid and connected with a mercury manometer; the solutions were injected into the jugular vein. The results showed that sodium selenite and sodium tellurite have a greater effect upon the blood pressure than sodium selenate and sodium tellurate. The lowering of the blood pressure is due partly to the lowered tone of the vessels of the splanchnic area and partly to the cardiac paralysis.

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**Observations upon the Resistance of the Rat to Consecutive Injections of Strychnin.**

*Erich W. Schwartze, J. Pharmacol. & Exper. Ther., 19:49, Feb., 1922.*

The experiments were planned so that some idea could be obtained of the resistance of the rat as judged by the relation of survivals to fatalities in a given series, as well as by the coefficients determined arithmetically for each individual animal. The purpose of the first type of evidence was to serve as a check, since the second method tended to give low results unless the strychninization had been continuously kept up almost to the possible maximum. Accordingly a large number of rats were consecutively injected with the minimum lethal subcutaneous dose of strychnin sulphate (3 mg. per kilo in 0.1% centration). The survivors were tested at two-hour intervals with fractional multiples of this dose. The experiments were performed practically simultaneously, and the same syringe, solutions and technic were used. The results of a number of experiments in which strychnin was administered orally were also briefly reported. All the administrations were made by means of the stomach tube (urethral catheter) and a record syringe, lightly etherized rats being used as subjects. The strychnin was in the following forms: the sulphate in solution, the alkaloid in 100 fine powder suspended uniformly in starch paste, and the sulphate dissolved in an aqueous solution of the food color amaranth. The results of the injections at the beginning of the third hour, as judged by fatalities and survivals, indicated that approximately half of the rats will dispose of 50% of subcutaneous minimum lethal dose in two hours, and will all presumably dispose of 33%, and that occasionally one will dispose of 67%.

Evidence was adduced showing that the coefficients of disposal, which are necessarily expressed in terms of percentage of minimum lethal dose per given period of two hours, are too low. They should be reinterpreted to fit the case of oral administration in which large amounts are administered at once and in which type of experiment the absorption of strychnin has an opportunity to keep pace with the disposal. Accordingly, the coefficient disposal has been regarded as constant, and the absolute amount disposed of as a variable depending upon the amount present. On this basis the disposal of strychnin by the rat may reach at least 1 mg. per kilo per hour. This occurs only when the strychninization is kept constantly very close to the maximum

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limit, by absorption from the gastro-intestinal tract. The extremely high tolerance of the rat (as well as of other animals) to consecutive injections of strychnin would seem to be significant in respect to the possibility of correlating this with the failure to demonstrate an habituation to this drug.

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**Taxin, an Alkaloid Prepared from Taxus Baccata (Yew).**

*E. Winterstein and D. Jatrides, Hoppe-Seyler's, Ztschr. f. physiol. Chem., 117:240, Berlin, Dec. 27, 1921.*

For the preparation of taxin, 15 kg. needles of green twigs were stirred repeatedly with 90 liters 1% sulphuric acid and allowed to stand several weeks. The brown, turbid liquid is previously filtered and alkalized with 2-3 liters ammonia and shaken with 4 liters ether. To the clear ethereal solution 50-60 c.c. sulphuric acid (1%) is added and taxin liberated with caustic soda and taken up in ether. The ether is evaporated in a vacuum desiccator. The residual white scaly mass is taxin. The yield on repeated extraction of the same taxus needles is 0.66% to 1.38% taxin. The fruit kernels contain 0.25% taxin.

Taxin is soluble in the common solvents, excepting benzin, which precipitates it from solutions. The melting point of the new substance is about 97° C. Among many color reactions may be mentioned the reddish violet color with sulphuric acid, and blue with sulphuric acid, and blue with sulphuric acid and potassium bichromate. From elementary analysis the formula  $C_{37} H_{51} O_{10}$  is obtained. The alkaloid may be split up by organic and inorganic acids with production of cinnamic acid, acetic acid, a resinous substance (yield about 50%) and an imperfectly known reducing substance. The resinous substance is free from nitrogen and unsaturated. Cinnamic acid is also obtained by treating taxin with cold caustic soda but not with warm caustic soda. If taxin is treated with acetic anhydrid (two hours with the reflux cooler) a compound having 3-4 acetyl groups is obtained. The splitting up of the alcoholic dilution also produces cinnamic acid. Taxin possesses strong reducing properties. With ammoniacal silver nitrate it gives a silver mirror and reduces Fehling's solution. Treated with boric acid taxin takes up two molecules. With methyl iodid it is converted into taxin methyliodid, which, on addition of caustic soda, decomposes with formation of trimethylamin and a body having the formula  $C_{37} H_{41} O_{10}$ . When a 29% taxin solution was allowed to stand three months with perhydrol a small amount of crystalline substance was obtained which is being investigated further. On treating taxin with perhydrol at room temperature for two months and warming the solution with concentrated hydrochloric acid and phloroglucin a yellow crystalline body was formed; this could not be studied more closely as the conditions of its formation were not fully known. Oxidation with potassium permanganate yielded benzoic acid, benzonitrol, acetic acid, oxalic acid and a reducing substance giving with phenylhydrazin a substance with the formula  $C_4 H_8 ON$ . The constitution of taxin was partially determined. It contains 37 carbon atoms of which 9 fall to cinnamic acid, 7 to residual benzol and 2 to acetic acid. On distillation with zinc dust at 300° C. no heterocyclic bases were formed. The lethal dose for rabbits was 0.004-0.005 gm. taxin intravenously per kilogram of body-weight. In dogs the lethal dose was 0.009 gm. intraperitoneally per

kilogram. In rabbits the lethal dose, intra-orally, was 0.024 gm. per kilogram. The toxic effects are diastolic arrest of the heart action, reduction of blood pressure, increase in frequency of respiration and pulse, acceleration of intestinal function, spasms of the posterior extremities, disturbances of equilibrium, comatose condition and, finally, death.

(1c—158)

**The Influence of Lecithin on the Excretion of Veronal.**

*O. Bachem, Biochem. Ztschr., 126:117, Berlin, Dec. 27, 1921.*

Since the formulation, by Mayer and Overton, of the theory of the affinity of the narcotics for the lipoids, the detoxicating action of lecithin has frequently been studied. The subject of this study is the examination of the influence of lecithin upon the soporifics proper in the rabbit, veronal being employed; 5 c.c. of a 19% lecithin emulsion were injected subcutaneously or intravenously into the animals. Depending upon the experimental conditions, 0.3-1 gm. veronal sodium in a 10% solution was always simultaneously administered by subcutaneous injection. With equal quantities of veronal the advent or duration of sleep did not exhibit any significant differences. The animals fell asleep one-half an hour after the injection, and were awake again but still in a condition of somnolence after twenty-four hours. Differences in the excretion, however, were noticed, according to whether the veronal sodium had been injected subcutaneously or intravenously.

**Results:** After subcutaneous injection of a mixture of lecithin and veronal sodium the excretion of veronal is about the same as after the injection of veronal sodium alone; if, however, the lecithin is injected intravenously and the veronal sodium subcutaneously, the veronal excretion diminishes considerably within four days, amounting to only about one-half or one-third of the normal.

This phenomenon may be explained by assuming that the intravenously injected lecithin is distributed in the blood, in the brain and other lipoid-containing tissues, whereby the lecithin content of these tissues is increased and the fixation of the veronal facilitated and accelerated.

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**What Ought the United States Pharmacopeia to Contain?**

*Oliver T. Osborne, J. A. M. A., 78:639, March 4, 1922.*

The writer wishes to urge the present revision committee to make this pharmacopeia of small size, a standard for useful drugs. He offers a list of substances, drugs and preparations which may well be deleted. It is useless to attempt to standardize what cannot be standardized, and thus detract from the remainder of this scientific book of standards. Four tables accompany this article: (1) substances recommended for deletion because they cannot be standardized; (2) spices which should be deleted; (3) chemicals which should be deleted; and (4) drugs and preparations which should be deleted. Osborne thinks that the revision committee should allow its physicians to decide what drugs are needed in the pharmacopeia. The decision should not be left to the pharmacists or to the pharmaceutical chemists. After the physicians decide on the drugs they want, scientific pharmacists should decide the assays necessary to secure standards and purity of these drugs. The phar-

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maceutical and chemical experts should then decide upon the most efficient and the pleasantest preparations, while the dosage should be agreed on by pharmacologists and clinicians jointly.

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### Lethal Dose of Arsenic.

*G. Joachimoglu, Klin. Wchnschr., 1:169, Berlin, Jan. 21, 1922.*

Joachimoglu makes a compilation of 7 cases taken from literature, in which the taking of large amounts of arsenic, up to 60 gm., did not cause death; but in every case (with the exception of that of one arsenic-eater) the patient vomited, and it is therefore difficult to determine from them exactly the effective dose. One case of his own is reported, in which the patient took 12 gm. arsenic together with 1.4 gm. morphin. Neither vomiting nor diarrhea occurred, probably on account of the morphin, and the stomach was pumped out after twenty-four hours. Poly-neurotic symptoms developed and recovery was not complete for nine months. The patient's hair gave a distinct arsenical reaction three months after the poisoning, but none after nine months.

In cases of arsenic-poisoning the poison can always be detected in the hair, provided not too long a time (nine to ten months) has elapsed since the poisoning; this reaction never fails.

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### Symptoms and Pathology of Collargol Poisoning in Man.

*F. Herzog and A. Roscher, Virchow's Arch. f. path. Anat., etc., 236:361, Berlin, Jan. 14, 1922.*

The employment of silver preparations, especially of collargol, in septic processes has been in vogue for a considerable time. Recently there has been a revival of the advocacy of intravenous injections of collargol and other silver products in gonorrhea, and in quite high dosage. B. Zieler, for instance, recommends single injections of 50 c.c. daily, for five to seven days in succession. That at times the intravenous administration of collargol is not altogether harmless is shown by the fatal outcome in 2 cases of collargol poisoning. The patients were both girls, 21 years old, suffering from both syphilitic and gonorrhreal infections. In both there were severe general reactions after the collargol injections, with chills, fever and severe purpura. Histologically there was marked involvement of the bone marrow, local hemorrhages, and necroses, explaining the thrombopenia and purpura. In the second of the 2 cases the affection of the bone marrow was so severe as to lead to a complete myelophthisis. Numerous changes in the structure of the blood-vessel walls account for the hemorrhages. There were deposits of collargol in all organs with severe destruction of tissue in the bone marrow, and necroses in the liver, spleen and kidneys. In order to determine whether these tissue lesions were caused by the collargol or the arsphenamin administered to the patients, animal experiments were instituted. However, the course of the illness points rather strongly to a diagnosis of collargol poisoning. As to the behavior of collargol in the tissues, it was shown that the small particles found in the solutions used for injections gradually enlarge to bigger particles, and are phagocytized. Very frequently there is a deposition of

silver granules on the connective tissue fibres. Various alterations in the blood-vessel walls, thus demonstrated, account for at least part of the hemorrhage caused.

Collargol, therefore, like benzol, the x-rays and salvarsan, may under certain circumstances lead to severe purpura and affections of the bone marrow. It is recommended that the use of large doses of collargol, especially in high concentration, be resorted to with caution.

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**Action of Cyanamid.**

Erich Hesse, *Ztschr. f. d. ges. exper. Med.*, 25:321, Berlin, Dec. 15, 1921.

Individuals who inspire calcium cyanamid in the course of their occupation show disease symptoms only if they consume alcohol. The symptoms of calcium cyanamid poisoning consist in brief attacks of general weakness with quickened respiration, rapid heart action, lowered blood pressure and a transitory exanthem confined to the head and chest. Cyanamid, ( $\text{HN}-\text{C}=\text{NH}$ ), the most important toxic factor of calcium cyanamid, was investigated by the author from the toxicologic standpoint. In the frog the administration of cyanamid leads to diastolic arrest of the heart's action, which is influenced only by intraperitoneal injection of adrenalin. The attacking point of the toxic action is the intraventricular automatic apparatus. In the rabbit 0.2 gm. cyanamid per kilo body weight reduces temperature, while 0.4 gm. per kilo causes death. Intravenous injection produces irregularity of the pulse with slowing and plateau formation at the height of the systole. No lowering of blood pressure takes place. Chronic administration of sublethal doses has no cumulative action, but leads to much loss of weight. In dogs and cats pareses, tremor, vomiting and diarrhea appear. A metabolism experiment showed increase of creatin and creatinin and excretion of cyanamid as uric acid. Attempts to render cyanamid nonpoisonous in the animal organism by pairing it with sarcosin and glycocoll gave negative results. Combinations of cyanamid and alcohol, in warm-blooded animals, did not increase the toxic action of the heart, but blood pressure was lowered to a greater extent than with administration of the same amount of alcohol alone. Alcohol administered after cyanamid lowered temperature much more than cyanamid alone. To determine whether the action of cyanamid in combination is exerted peripherally or centrally on the vessels, Hesse tried the combination of substances possessing special peripheral action (such as yohimbin), or central action (like alcohol), with a group of narcotics (veronal, urethan), and with pyramidon and sodium nitrite. Only small doses were given of these agents, which have no effect on temperature, and the experiment with previous administration of cyanamid was repeated. The action of alcohols, yohimbin and chloral hydrate was reinforced by cyanamid; this does not decide the question of a peripheral or central action. In the investigation of the combined action on the smooth intestinal musculature, Hesse sometimes employed cyanamid alone and at other times inactive doses of substances stimulating smooth muscle (pilocarpin, physostigmin) and such as paralyze it (papaverin, atropin). The action of the former was not promoted; but that of the latter was increased remarkably, particularly in the case of codein and morphin, which themselves possess only a slight paralyzing action. In order to

examine a further peripheral function Hesse endeavored to increase the diuretic action of the purin bodies by cyanamid. These experiments showed that inactive doses of theobromin were transformed into active ones by cyanamid. The experiments on the intestines and kidneys point to a peripheral attacking point for cyanamid; but in view of the experiences with alcohols, it seems more probable that cyanamid in nerve poisons acts chiefly centrally.

Owing to the rapid elimination of cyanamid, the phenomena of calcium cyanamid poisoning are transitory. For the prevention of this industrial disease, the admixture of various oils is to be advocated, to lessen the splitting of calcium cyanamid; the workmen employed in these pursuits should be enjoined to avoid the use of alcohol before and during their work. In experiments on a healthy individual, to investigate the therapeutic use of cyanamid in man, 150 mg., orally, were tolerated well. The individual in question, to whom this dose was given in the forenoon, became ill in the evening after taking a glass of beer, complaining of headache nausea and the typical exanthem. These symptoms disappeared after a few hours.

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**Rapidly Fatal Poisoning with Cyanid of Mercury.**

*R. Lakaye, Arch. méd. belges, 74:1129, Liège, Dec., 1921.*

The poisoning occurred in a tabetic woman of 62. As pains in the legs were especially troublesome, treatment with mercury was instituted. An injection of 1 cg. of the cyanid was well supported and was followed in two days by another of 1.5 cg., which was equally well borne. In another two days, the patient again received 1.5 cgr. Some six to ten hours later, the patient was seized with colic and diarrhea, and had two violent intestinal hemorrhages. About eighteen hours after the injection, collapse and death occurred. The striking features of the case are the rapid intoxication without warning signs, and the small dose causing death. Mercuric cyanid should, therefore, be used with great caution. The gums should be systematically examined and inquiry made for intestinal symptoms. Treatment should be stopped on the appearance of the least suspicious sign. However, mercuric cyanid is very active, and is easy to manage, and Lackaye remains a thorough believer in its use.

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**Chlorin and Hydrogen Metabolism in Sublimate Poisoning. Observations Regarding the Calcination Technic of the Organs of Animals for the Chlorin Test.**

*A. Bornstein and Joh. Kerb, Biochem. Ztschr., 126:120, Berlin, Dec. 27, 1921.*

Experiments undertaken by Walgren on the subject of the chlorid content of all the organs of an animal were tried on the organs of normally fed dogs and on the organs of dogs which two hours before death had received an intravenous injection of hypertonic NaCl solution. The greatest percentage chlorid content was in the skin, blood, kidney and lung. The lowest was in the muscles. The greatest per cent. of chlorid increase was found in the lung, intestine, blood, skin and kidney. According to Walgren's figures the greatest quantities of chlorid are deposited in the musculature, where they are almost twice as great as

in the skin, the organ most rich in chlorin. Experiments were made with animals which showed toxic kidney changes. Rats, usually during one analysis, were first used. Before killing, they were starved 3 times for twenty-four hours. The NaCl animals received after every twenty-four and forty-eight hours 1 mg. NaCl per kilo, subcutaneously. The kidney damage resulting from the sublimate produced in all cases a necrosis of the epithelium of the convoluted tubules. The chlorid test was used with titration according to Mohr. The experiments show the figures for normal cases given by Wahlgren as regards the percentage content chlorid. Brain, liver and muscle represented the organs with the poorest percentage of chlorid. The organ richest in chlorid was the skin, then followed the blood, skeleton, lungs, kidney. In animals poisoned by sublimate it was shown that upon introduction of a large quantity of common salt, an important increase in the chlorid content of the musculature follows. The chlorid content of the skin is, on the other hand, increased in very slight degree. In this case, the skin appears as the greatest depositary for water.

In order to find whether the retention of water and sodium chlorid would occur similarly in the case of other kidney poisons, a series of tests were made with cantharidin. It appeared that the chlorid retention in the cantharidin experiments was much smaller than in the sublimate animals, although the anatomic changes in the kidneys were much more marked than in the kidneys of the sublimate animals. In animals poisoned by uranius, there resulted a pure chlorid retention in the tissues, while the water content did not increase. Here also the independence of the water from the chlorid retention was demonstrated, since water was deposited only in the serous cavities and the chlorid in the skin and musculature. Contrary to the case in poisoning by cantharidin, the chlorid content of the blood was increased; in contrast to that in sublimate poisoning, the water content of the skin was not increased, but only that of the serous membranes. Consequently, it may be concluded that the localization of the deposit is different for the different poisonings; that chlorid and water are very seldom retained together in the same organs; that the musculature and skin play a special rôle in the depositing of the chlorid and, finally, that the extent of the retention is not parallel to the microscopic changes in the kidneys.

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#### Clinical and Experimental Data on the Toxic Action of Quinidin.

*Walter Frey and E. Hagemann, Ztschr. f. d. ges. exper. Med., 25:290, Berlin, Dec. 15, 1921.*

In 4 cases of total cardiac arrhythmia there were observed severe symptoms that were certainly related to the action of the quinidin employed in the treatment. A man aged 63 was suffering from indurative myocarditis. After reestablishment of normal pulsation a lung infarct appeared, obviously as a result of the detachment of a thrombus situated in the right heart. Danger of embolism with its doubtful prognosis always exists in such patients. The paralyzing action of quinidin on the cardiac muscle, which is the foundation for its employment in fibrillation as a condition of extreme hyperkinesis shows that the paralysis of respiration originates in the heart. In order to decide the attacking

point of the quinidin action experiments were carried out on rabbits which justify the assumption of a primary cardiac injury with secondary arrest of respiration. In such conditions of collapse following administration of quinidin, nothing can be expected of digitalis and strophanthin. Camphor and adrenalin are recommended.

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**Experimental Generalized Analgesia after Exposure to Some War Gases.**

*John Auer, J. Exper. Med., 35:97, Feb., 1922.*

Exposure to dimethylsulphate and chloropicrin was found to cause analgesia so profound that laparotomy could be performed. In cats exposed to the vapors of these substances, analgesia was well established in a few hours and reached a maximum in twenty-four hours. With dimethylsulphate the analgesia may last six months, with chloropicrin about seven days. The analgesia is considered to be caused and maintained largely by a general, low grade tissue asphyxia which is chiefly of pulmonic origin.

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**The Vitamin Content of Microorganisms in Relation to the Composition of the Culture Medium.**

*C. Eijkman, C. J. C. van Hoogenhuijze, and T. J. G. Derkx, J. Biol. Chem., 50:311, Feb., 1922.*

One of the authors attempted to isolate the antineuritic factor from an aqueous solution of extract of rice polishings by removing the sugars through the agency of yeast, but the result was that the medium had lost its antineuritic properties. This experience, in combination with the fact that bakers' as well as brewers' yeast is obtained by cultivating them in media originally containing vitamin, gave rise to the supposition that the yeast cell may not be able to synthetize the vitamin but may take it as such from the medium. Subsequently yeast species cultivated at 27° C. in vitamin-free media, proved in experiments on polyneuritic fowls to fail in curative effect. On the other hand, control experiments with the same species of bakers' yeast cultivated at 27° C. in aqueous solution of extract of rice polishings, after washing with physiological salt solution in order to remove the adherent traces of the medium, gave a distinctly positive result. This aqueous extract had been previously divided into 2 portions, one of which was boiled for a short time only and then filtered and inoculated with the yeast, whereas the other portion was heated before filtering for one hour in the autoclave at 120° C. in order to destroy the antineuritic factor. Both of these yielded highly active yeast, but the liquids, separated from the yeast at the end of the fermentation, were found to be inactive. In the opinion of the authors it seems, therefore, that yeast not only takes eventually its antineuritic factor as such from the culture medium but that it is not even capable of synthetizing the vitamin unless the medium contains at least the products of decomposition of the vitamin by heating.

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The authors also demonstrated experimentally that *B. coli communis*, even after having been cultivated in a medium which contains the antineuritic factor, remains devoid of this vitamin. The antineuritic factor and the growth-promoting, water-soluble B substance are not identical.

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### **Albumin-Free Agar-Agar.**

*Klostermann, Ztschr. f. Hyg. u. Infektionskrankh., 94:262, Berlin.  
Dec. 2, 1921.*

The chemical composition of agar-agar, is variable, because the alga from which it is derived are not always similarly combined. The content of nitrogenous substances varies between 2.53% and 11%. For certain anaphylactic experiments it was necessary to produce agar-agar which was free from albumin. There were 2 possible methods: (1) to eliminate the nitrogenous substances and leave the other substances untouched; (2) to produce nitrogen-free extractive substances through elimination of nitrogenous substances.

The first method was selected; 30 gm. were mixed with from four to five-fold volume of 8% alcoholic solution of potassium hydroxid and kept for some time in a temperature of from 60° to 70° C. The mixture was kept for some days and the lye was eliminated from the agar by means of suction; this agar was washed with alcohol and treated with from two to four-fold quantity of 8% KOH. This treatment was repeated 3 times. The residuum was treated 3 times with pure alcohol, and after that with slightly acetic alcohol, the solution was filtrated and the agar dried carefully in a temperature of from 60° to 70° C. The purified agar dissolved perfectly clear and its 0.5% solution solidified very well, which fact suggested that the physical qualities of the gelatinous substances had not changed. The ninhydrin, biuret and xanthoprotein reactions were negative. No Berlin blue was formed when Lassaigné's method was followed. The experiments demonstrated that the solidifying capacity of the agar does not depend upon the albuminous substances. To the albumin-free starch of Möser, Kopaczewski's albumin-free pectin substance, and also mother's milk must also be added albumin-free agar. The latter may be substituted for celic acid medium, which is free from albumin and carbohydrates, in case a medium lacking albumin but not carbohydrates is required.

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### **Sulphur in Agar.**

*Carl Neuberg and Hans Ohle, Biochem. Ztschr., 125:311, Berlin,  
Dec. 18, 1921.*

In the cultivation of microorganisms on agar an odor of hydrogen sulphid is perceived, although the addition of organic or inorganic combined sulphur was wholly excluded. The examination showed agar to be free from mineral sulphur compounds but that it split off sulphuric acid on hydrolysis with hydrochloric acid. This behavior pointed to the presence in agar of a paired sulphuric acid possibly in the form of a carbohydrate-sulphuric acid ester, or of a nitrogenous chondroitin-sulphuric acid. According to Tamman ether-sulphuric acids have been found in yellow peas and according to Smith glucosidal combina-

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tions of sulphuric acid occur in crucifer seeds. After decomposition with hydrochloric acid and precipitation with barium chlorid the detection of sulphuric acid was possible. It was also found in the product of dry distillation by treatment with tenth-normal caustic soda. From this it seemed as if sulphuric acid participates in the souring of nutrient agar mediums. If high molecular sugar varieties combine with sulphuric acid esters this combination would be parallel to the natural carbohydrate-phosphoric acid esters to which starch belongs.

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**The Action of Dilute Acids upon Bacterial Growth in Optimum Hydrogen Ion Concentration.**

*I. Walker Hall and A. D. Fraser, J. Path. & Bacteriol., 25:19, Edinburgh, Jan., 1922.*

The object of these experiments was to determine the rate of growth of various organisms in media of definite pH concentration in the presence of varying acids. The subject was approached from the standpoint of total, or hourly, generations at the first maximal period of growth. The medium employed throughout the tests was a peptone solution prepared from pure casein adjusted to a content of 20n/10 amino-acid. This was made neutral to phenolphthalein with NaOH, then neutralized to pH 7.6 by the addition of n/HCl,HNO<sub>3</sub>. The amount of the acid employed was calculated, so that the quantity present in each culture tube was known. The period of maximal increase was determined for each organism, the enumerations were made on 3 daily successive batches, and the pH narrowed to the range associated with the smallest pH alteration. The technic in preparing cultures and plates and throughout the experiments was adapted to allow for errors associated with the age of the organisms, the amount of inoculum, and the precise stage of bacterial growth. It was found that by using pH 7.6 casein medium containing dilute amounts of various acids, the period of logarithmic increase may be altered. A study of the tables shows that the individual bacteria vary in their response to the accelerating or retarding influences, but the presence of lactic or nitric acids in dilutions of 1 in 166 acts generally as a stimulus to growth, while salicylic, butyric and phosphoric delay the period.

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**The Alkalinity of Culture Mediums, Measured According to Michaelis' Indicator Method, in Its Relations to the Growth of Bacteria.**

*Stickdorn, Ztschr. f. Immunitätsf. u. exper. Ther., 33:576, Jena, Jan. 19, 1922.*

As indicator of the pH of culture media, metanitrophenol has one advantage over phenolphthalein and litmus. By watching and comparing the color differences (the culture media in small tubes being viewed against a mat and a blue disk) one can obviate inconveniences in examining dark culture media. The media were mixed with a 0.3% NaCl solution and 0.2% Na<sub>2</sub>HPO<sub>4</sub>, and alkalized with NaOH. The bouillon thus produced showed the following degrees of alkalinity: pH 6.8, 7, 7.2, 7.4, 7.6, 7.8, 8, 8.2, 8.4. After being sterilized twice, which

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only caused a slight decrease of alkalinity in some cases (not under pH 0.2), the various kinds of bouillon were inoculated with 21 species of bacteria. It was found most bacteria grow in the alkalinity of spring water (pH 7.5); most of them have a considerable range. Streptococci and anthrax require a somewhat more strongly alkaline culture medium. With the exception of *Bacillus typhosus*, *B. alcaligenes*, *Streptococcus*, *B. erysipelatos suis* and *B. septicaemiae haemorrhagiae*, all bacteria continue to show satisfactory growth at pH 8.0. A bouillon of pH 7.5 is therefore to be recommended as a general culture medium.

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**Some Bacterial Proteases Endowed with Extracellular Action.**

*K. G. Dernby, Biochem. Ztschr., 126:105, Berlin, Dec. 27, 1921.*

Nearly all microorganisms contain proteolytic enzymes, some more, others less. The attempt was made to determine which bacteria possess proteolytic enzymes exhibiting an extracellular action and what properties are characteristic for those enzymes. The following procedure was employed: The bacteria to be tested were cultivated in broth and filtered and the sterile filtrate was examined as to the possible presence of enzymes. Gelatin was used as an indicator for proteolytic enzymes. The gelatin test was carried out in the modification introduced by Palitsch and Walbum.

The peptone test consisted in adding bacterial filtrate to a solution of pepton, the hydrogen ion concentration of which was varied by means of addition of HCl and NaOH. The pepton was broken down by means of the formol method of Störensen.

In order to determine the optimum of reactivity of the enzymes with regard to peptone and gelatin, the pH was controlled according to the colorimetric method of Sörensen. For tubercle bacilli, pneumococci, streptococci, staphylococci, and tetanus bacilli, the tests were negative. The following bacteria contained strongly active proteolytic ferment: *Bacillus subtilis*, *B. pyocyanus*, *B. proteus*, *B. prodigiosus*, *B. sporogenes* and *B. histolyticus*. For all of these organisms, the pH values were found to be between 6 and 7 in the gelatin test as well as in the peptone test; in other words, the optimum for these organisms is located at the neutral point. The range of the pH for all the enzymes is very wide, between 4 and 9. In the experiments on proteolytic enzymes of yeast the following enzymes could be distinguished: (1) enzymes resembling pepsin, with an optimal action at pH 4.5, and attacking egg-albumen and gelatin; (2) a trypsin group, with an optimum, for the breaking down of peptone, casein and gelatin, at pH 7; (3) ereptases breaking down glycylglycin, whose optimum was at pH 7.8. Such an analogy of enzymes was not found in the bacteria mentioned above.

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**The Formation of Phenol by Bacteria.**

*Fritz Sieke, Ztschr. f. Hyg. u. Infektionskrankh., 94:214, Berlin. Dec. 2, 1921.*

Frieberg isolated from human stools a series of *Bacillus coli* strains which he designated as *Bacterium coli phenogenes*, as they were capable of forming phenol. The breaking down of proteins through putrefaction and digestion finally produces phenol in the

human intestine. Of the amino-acids derived from proteins, tyrosin is the p-oxyphenylaminopropionic acid attacked by the bacterial action in the alanin side chain, which in splitting releases phenol. The splitting is analogous to the alanin side chain splitting of tryptophan in the formation of indol. The presence of phenol formed through bacterial action is proved by adding bromin water to a protein-free solution; tribromphenolbrom is produced. The fluid containing phenol and free from protein, gives a dark red color with Millon's reagent. If fluid containing phenol is diluted with from 1 to 2 drops of 10% formaldehyd solution and stratified with sulphuric acid, a red violet ring arises at the point of contact; the color of the ring is brown if paracresol is present (Marquis' method). If about 0.1 c.c. 10% NaOH, 0.5 c.c. 0.5% para-amidophenol solution (freshly prepared) is added to 10 c.c. of a culture, a dark blue ring is formed at the point of contact after stratification with a few drops of sodium hypochlorid, if phenol is present. It is possible to perform this Berthelot-Lex reaction as well as Marquis' reaction in the culture itself. To prove the presence of phenol in a solution, it is necessary to distil the solution after it has been rendered slightly alkaline. The phenol appears very early in the reaction. The distillation can be omitted, but it is then necessary to extract the phenol by means of ether. As the substances formed from tyrosin were demonstrated by means of the known reactions, which are group reactions, other products, chemically related to phenol, may also have been present. The antibacterial effect of the substance formed by the bacteria was therefore also proven. As the phenol formed in a culture of an organism producing phenol is not bacteriolytic in its weak concentration, a stronger concentration is necessary, and may be obtained through distillation. Bactericidal experiments were performed on bouillon cultures of staphylococci. A gradual but distinct decrease of the organisms was observed in the culture tube to which phenol distillate had been added, and no viable organisms could be found after forty-eight hours. This establishes the biologic proof of the bacteriolytic action of the distillate.

As the bacteria break down tyrosin into phenol, it is necessary to provide the former in the form of a suitable culture solution. The so-called tyrosin water is especially suited for this purpose; this contains only chemically known substances which are absolutely necessary for the life of the bacteria, and tyrosin. The composition is as follows: 0.3 gm. tyrosin, 5 gm. asparagin, 5 c.c. ammonium lactate, 0.2 gm. magnesium sulphate, 2 gm. potassium phosphate and 1000 c.c. distilled water. This tyrosin water is surpassed by trypsin bouillon and tyrosin (0.3 gm. tyrosin to 1000) for the culture of phenol-forming bacteria. To examine a bacterial culture as to its production of phenol, the culture is inoculated into 10 c.c. tyrosin-trypsin bouillon, left to stand for forty-eight hours, the test is then performed in the culture, which has been cooled to 10° C. The following bacterial strains were found not to form phenol: 4 typhoid, 2 paratyphoid A, 3 paratyphoid B, 7 staphylococci, 8 anthrax strains, 2 hay bacilli, 7 sarcinae, 9 various dysentery strains, 12 various coli strains, 4 cholera strains, 4 proteus strains, 2 Bacillus alkaligenes strains, 5 bacilli of Friedlander's group, 4 pyocyanus strains, 5 streptococci, 3 rat bacilli, erysipelatous bacilli, prodigiosus, xerosis, plague, Bacillus suipestifer, Diplococcus Morax-Axenfeld, Bacillus mallei and many other less important strains.

The pure culturing of the strains forming phenol was usually performed in the following manner: the material to be examined, generally stools, was inoculated with Endo's agar on a slide sediment. Thence various colonies were inoculated into separate tyrosin-water tubes, on the basis form, color and size. These individual tubes were examined after an incubation period of two days, for the presence of phenol. If the strain could not be defined as pure the phenologenic strain was placed on an Endo's agar slide divided into 3 parts. *Bacterium coli phenogenes* was isolated in the following manner: small, Gram negative motile rods, dark red colonies on Endo's agar; the vicinity of colonies reddened by lactose fermentation; good growth on Löffler's serum; no liquefaction; no formation of indol in the trypsin bouillon; the gelatin liquefied; the litmus milk distinctly reddened. An isolated *Bacterium paracoli phenogenes* was distinguished from the species described in that it fermented lactose only slightly. It was possible, by means of immune serum prepared from the strains, to demonstrate that the 2 strains, *B. coli phenogenes* and *B. paracoli phenogenes* are separate independent species of the *B. coli* group. As regards the spread of these phenologenic strains, it was possible to determine that the bacilli were present in about 85% of 35 healthy individuals and of 100 sick ones. It was not possible to determine the cause of the lack or the accumulation of the bacilli during certain diseases; neither could the influence of nourishment be demonstrated. Phenogenic strains were also found in animals, especially in carnivora. Two phenogenic coli strains were also isolated from 2 samples of water. A test showed that a permanent incorporation into the intestinal flora of an exogenous artificially inoculated bacterial strain is not possible. No phenogenic bacteria were found in the stools four days after the ingestion of *B. coli phenogenes*. Coli strains capable of forming phenol from tyrosin exist in 85% of all human beings as regular inhabitants of the intestine. All bacterial strains capable of forming phenol are Gram negative, as are also the indol-forming bacteria. Three strains of chicken cholera and 2 strains of Perez's ozena bacilli were found to be phenogenic.

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**A Simple Method for Anaërobic Cultivation in Petri Dishes.**  
*Sterne Morse and Nicholas Kopeloff, Am. J. Pub. Health, 12:119, Feb., 1922.*

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The procedure for anaërobic cultivation consists in placing 2 sterile Petri dishes of uniform diameter edge to edge with a strip of surgeon's adhesive plaster around the joining of the two. In the upper Petri dish hangs the culture medium with the culture; in the lower, 5-10 gm. dry powdered pyrogallic acid and about 30 c.c. NaOH 5%. That the conditions are anaërobic is proved by success in the culture of *Bacillus tetanus* and *Bacillus putrificus* and the power to reduce methylene-blue when used as an indicator of anaërobiosis. A good growth of *B. tetanus* was obtained, however, only when 2% glycerin was added to the agar medium, this combating the strong dehydrating effect of the pyrogallic acid.

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**The Staining of the Flagella of Bacteria.**

*Gianni Petragnani, Policlinico (Med. Sect.), 39:30, Rome, Jan. 1, 1922.*

Petragnani describes his own method for demonstrating easily and rapidly the eventual elongation of the bodies of bacteria. The culture of the bacterium whose flagella are to be studied should be made on a ground of agar, obtained from Löffler's broth with peptone 1.1%, sodium chloride 0.5%, and agar agar 2%. The reaction should be slightly alkaline to litmus (below the neutral point of phenolphthalein). The temperature should be that best suited for the development of the bacterium, and the culture should be considered sufficiently developed when a thin stratum of bacterial film has been formed on the surface of the agar (fourteen to eighteen hours). A loopful of bacterial suspension in sterile water is placed upon well-cleaned cover-glasses and dried in a thermostat, and the macerating and fixing fluid applied. This is prepared as follows: In a test-tube are placed 3 gm. potassic alum and 0.5 gm. zinc acetate (well-triturated crystals), 3 drops of cold acetic acid, and 100 c.c. distilled water. This is then placed in a hot water-bath. When it is well dissolved and boiling, another solution is added, consisting of 7 gm. pure tannic acid with ether, 2 gm. well-conserved and pure ferric chlorid, 35 c.c. pure methyl alcohol, and 15 c.c. distilled water. The entire preparation is allowed to remain in the hot water-bath for several minutes, after which it is removed, closed tightly, and kept in a cool place. After two or three days it is poured through filter-paper and is then ready for use. About 15 drops of this liquid is poured over the preparation on the cover-glass, covering its entire surface. This is then allowed to remain at room temperature for twenty minutes to an hour. It is advisable to pour a few more drops of the liquid upon the glass when about half that time has passed. The glass, together with the preparation, is then well washed in water before the staining is begun. Into a watch-glass is poured a little anilin water (prepared by emulsifying pure anilin oil in distilled water to the point of saturation and then filtering it twice through filter-paper), and over this several drops of saturated alcoholic solution, of crystal violet or gentian violet, or of Ziehl's liquid. The preparation is kept heated with this solution for several minutes, then washed, mounted with balsam, and examined.

When the preparation so treated, through lack of care either in cleaning the glass or in the preparation of the bacterial suspension, does not present a sufficiently limpid field, this disadvantage may be obviated by placing it, already washed and stained, in a clearing solution consisting of 7 gm. chemically pure tannin with ether, 2 c.c. pure formalin, 1 c.c. pure phenol, and 100 c.c. distilled water. It may remain immersed in this liquid until the glass appears diaphanous and clear. It is then washed well in water and stained as described above. This clarifying bath, however, in clearing the field deprives the flagella of some of their relief; it must therefore be used with this fact in mind, and only in those cases where it has already been ascertained that the bacterium has visible flagella. As the liquid grows older it may lose some of its mordant qualities, but it has the advantage of producing clearer preparations. If it does not produce results promptly, a little heating will secure the desired effect.

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**The Use of Phenol Red and Brom-Cresol Purple as Indicators in the Bacteriologic Examination of Stools.**

*Alan M. Chesney, J. Exper. Med., 35:181, Feb., 1922.*

The author has used these 2 substances as indicators in the preparation of lactose-agar plates for the isolation of members of the colon-typhoid group of bacteria from stools. Of the 2, brom-cresol purple gives sharper differentiation and is to be preferred. They exercise no restraining influence upon the growth of cultures of the typhoid bacillus or paratyphoid bacillus freshly isolated from the human body, or of laboratory cultures of *Bacillus dysenteriae*. Both may be employed with brilliant green in the isolation of the typhoid-paratyphoid group from stools.

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**Relation between Saprophytism and Parasitism in Bacteria.**

*Katzumi Kojima, Klin. Wchnschr., 1:221, Berlin, Jan. 28, 1922.*

The double life of bacteria belonging to the group of gas bacilli has never been explained. As saprophytes they are chiefly producers of butyric acid, but in a wound they produce general toxic symptoms, gas phlegmon and gas edema. Katzumi Kojima studied Welch-Frankel's gas bacillus, which is a wide-spread saprophyte under the name of *Bacillus butyricus*. If a culture is made on a nutritive medium containing more than  $\frac{1}{2}\%$  grape sugar, and a filtrate of this culture is passed through a membranous filter, it is sterile but contains a toxin which kills mice almost instantly when injected intravenously; it can be heated to  $100^{\circ}$  without losing its effectiveness; but it was not possible to produce immunity or obtain a specific serum. It is capable of dialysis and is therefore not a true toxin. However, if a culture is made in a bouillon of lower grape sugar content (0.1-0.2%), to which a piece of muscle has been added, the filtrate contains a toxin which is destroyed at  $70^{\circ}$  and which is fatal to mice only after an incubation period of from several hours to a day, when 1 to 2 c.c. of it is given intravenously or 0.5 to 0.8 c.c. intraperitoneally. The animals can be immunized and their serum has a specific action against the toxin. This true bacterial toxin cannot be dialyzed. The bacillus as a saprophyte splits off substances resembling alkaloid or ptomain from its nutritive medium; but as a parasite it produces antigen or toxin, depending on the amount of carbohydrate in the nutrient medium. It becomes a parasite when, in addition to carbohydrate it obtains nitrogenous products, without changing its bacteriological characteristics. Muscle offers the best conditions for its parasitic development because of its chemical composition.

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**The Classification of Some Lactose-Fermenting Organisms Isolated from Cheeses, Waters and Milk.**

*T. Redman, J. Path. & Bacteriol., 25:63, Edinburgh, Jan., 1922.*

Redman isolated from the many samples taken from the various sources 66 trains of organisms. In some cases identical strains were isolated from the same source. MacConkey's method of classification was adopted. The strains found in Redmans investigation correspond culturally to numbers of MacConkey's classification and the sources

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from which they were obtained. The colon bacillus from bovine feces were divided into 2 classes according to their reaction on certain test substances. Class A, corresponding with groups 1 and 2, fermented dextrose, saccharose, lactose, raffinose, mannite, glycerol and usually dulcite, and almost invariably failed to utilize starch, inulin or adonite. Class B (group 3) failed to ferment saccharose, raffinose, starch and inulin. The colon bacteria from human feces agreed in most cultural reactions with those isolated from bovine feces. Making use of the correlated cultural reactions, only 20 cultures out of 66 might possibly have been due to fecal contamination of human or bovine origin. Of these cultures 14 were isolated from cheeses and 3 each from milks and waters. Many agglutination tests were made to find the relations existing between the different organisms isolated by the preparation of univalent antisera of these strains and their agglutinating powers were tested against each strain used for immunization. Certain strains were agglutinated by heterologous antisera, but it does not follow that the strains corresponding to the heterologous antisera react with an antisera to the first-mentioned strain. The strains are not agglutinated only by antisera to strains from the same source. With regard to different strains of organisms having the same cultural reactions, although their respective agglutinations with heterologous sera varied both in number and degree, yet there always occurred some reactions with a common antiserum or with antisera of closely allied strains. The strains differentiated from MacConkey's strains by cultural reactions are also differentiated by their agglutinations. In each group, a case or cases occurred in which agglutination occurred with heterologous antisera of another group but not of the same group. In groups 3 and 4, some strains were not agglutinated at all. Reactions with the antisera to coli from human feces took place chiefly with strains belonging to groups 3 and 4. The agglutination of strains of groups 1 and 2 are correlated with the Voges-Proskauer reaction. Strains of group 3 are not so correlated. The agglutination of strains of group 4 show this correlation with antisera to strains of groups 1, 2, 4, but not of group 3. Agglutination of strains are not correlated to so marked a degree with the indol reaction.

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**An Organism Resembling *Bacillus Actinoides* Isolated from Pneumonic Lungs of White Rats.**

*F. S. Jones, J. Exper. Med., 35:361, March 1, 1922.*

In the study of rat pneumonia Jones succeeded in obtaining from 11 cases organisms closely resembling those isolated by Theobald Smith from the pneumonic lungs of calves—*Bacillus actinoides*. *Bacillus actinoides*-like cultures were not obtained from every rat examined. In a few instances *Bacillus bronchisepticus* was isolated. Cultivation from the lungs of rats presents certain difficulties: The involved lobes are usually shrunken and afford very little material; the disease is a chronic one and affords excellent opportunity for invasion with more rapidly growing bacteria. Although such organisms have been observed in cultures from 11 cases, it is only with difficulty that they can be maintained. In several instances *Bacillus actinoides* was associated with a delicately growing streptococcus. It was possible to carry along these mixed cultures in serum media for several generations; ultimately only

the streptococci survived. These mixed cultures made the microscopic study difficult. It was only after a few pure cultures of the rods were obtained that the nature of the growth process became clear. In young cultures the organism appears as long slender bacillus. In older cultures on coagulated-serum media characteristic club-like capsular material is formed. On blood agar distinctive swellings appear at one or both ends of the rod. These become more refringent, and the body of the organism begins to shrink. Finally only rounded spore-like refringent bodies are found. The organism is Gramnegative.

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**Is Corynebacterium Abortus Infectiosi of Bang Pathogenic for Man?**

*M. Klimmer and H. Haupt, Münch. med. Wochenschr., 69:146, Feb. 3, 1922.*

Bang and Stribolt have shown that there is an infectious form of miscarriage in cows which runs a course like that of abortion. The cause is the *Bacillus sui corynebacterium abortus infectiosi* of Bang. Experiments have been carried out to determine its relation to similar conditions in other animals and in man. Artificial transfer and inoculation have demonstrated that *abortus bacillus* of Bang is pathogenic for nearly all mammals.

About 40% of the animals infected with this bacillus pass the *abortus bacillus* periodically for a long time. Bacilli were found in the milk in 32% of the cases. Milk which was proven to contain these bacilli may infect other animals, and the products of this milk, such as butter, cheese, or curds, are to be considered as similarly infected. The abortive effect of the bacillus is the most important effect; this was demonstrated in all the mammals which were examined. Many observers have pointed out that many healthy farmers wives aborted without demonstrable cause. Further examination revealed infection of the beef with the bacillus under discussion. The women in question had been drinking raw cow's milk. *Abortus bacilli* were found in the tonsils of children, and amoebocytes against *abortus bacillus* antigen could be demonstrated by the complement-fixation method. This leads to the assumption that *abortus bacilli* may find proper conditions for life in the human being, and that they can find their way from the gastro-intestinal tract into the rest of the body.

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**Cultivation of the Gonococcus.**

*Mary J. Erickson and Henry Albert, J. Infect. Dis., 30:268, March, 1922.*

Testicular blood agar with a reaction of pH 7.4 to 7.8 is found to be the most favorable medium for the isolation and cultivation of the gonococcus. Beef testicle from which all connective tissue has been removed is put through a meat grinder, weighed, and with twice its weight of distilled water added, is infused over night on ice. The following morning the mixture is heated in a double boiler to 50° C., allowed to stand for one hour, and then brought to the boiling point. It is then allowed to stand for another hour to permit the solid particles

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to settle, after which the liquor is decanted off and used as the infusion for the preparation of culture mediums.

For the preparation of testicular infusion agar, 2% peptone, 0.5% glucose, 0.2 to 0.3% monobasic sodium phosphate, and 2.5% granular agar are added. The mixture is heated over a flame and stirred constantly until the agar is dissolved. The medium is titrated with phenol red as an indicator and the reaction adjusted to pH 7.4 to 7.8; if phenolphthalein is used as an indicator, the adjustment is to a 0.6 reaction. The medium is tubed and autoclaved for twenty minutes at 15 lbs. The titration is checked after sterilization. While the tubes are still liquid (just before the agar solidifies) human blood in the proportion of 0.5 to 2.5% is added. If human blood is not available, defibrinated rabbit's blood (1 to 5%) may be substituted.

The absence of sodium chlorid, the proper reaction, and moisture content are especially important. Blood or blood serum mixed with the testicular agar or smeared on the surface of slanted tubes is necessary for the ready isolation of the gonococcus, but is not essential for the securing of growths of stock cultures. Fermentation tests made with solid mediums containing 0.5% glucose and phenol-red as an indicator result in a significant primary acidity and secondary alkalinity. Reduced oxygen tension is of no practical value for either the isolation or subsequent cultivation of the gonococcus. Anilin dyes of the violet and green colors tend to inhibit the growth of staphylococci more than that of gonococci from cases of mixed infection. Methyl violet added to blood-testicular agar in a proportion of 1:200,000 to 500,000 appears to be of the greatest value.

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**Further Note on the Cultivation of the Gonococcus.**

*C. E. Jenkins, J. Path. & Bacteriol., 25:105, Edinburgh, Jan., 1922.*

In a previous paper Jenkins showed that the water content of whole blood agar medium exercised a great influence upon the growth of the gonococcus. The present investigation was undertaken to find out the parts played by the blood and the nutrient agar in the medium, and to ascertain the reason, if any, for the high percentages of blood employed. The efficiency of the plasma of citrated blood was tested against whole blood and it was found that the former was not inferior in any respect; it was therefore used in the preparation of the medium. Agar slopes containing varying proportions of plasma were inoculated with 3 strains of gonococcus. These tests were repeated and each time it was found that the minimum proportion of plasma that gave maximum growth was 0.5%. The specific bodies in the blood that are necessary for the cultivation of the gonococcus are not destroyed by a temperature of 55°C. acting for twenty-four hours nor by sunlight. One sample was used with complete success when six weeks old, during which time it had stood on a window sill at room temperature and was exposed to sunlight. It was found that when beef extract was omitted from the medium, the proportion of plasma must be 5% or more. Peptone is not necessary when 1% plasma is used. When a dry sample of nutrient agar is used, the plasma present must be much higher than 1% to compensate for the lack of sufficient moisture. It is probable that where as much as 10 to 20% of blood has been found essential the unrecognised cause has been that nutrient agar was too hard, and that

most of the blood acted as a simple diluent. The following is the technic for plasma medium: (1) Nutrient agar of reaction 6 + (Eyre) and solidity 4. (2) Add to the medium 1% of plasma made with powdered sodium citrate, then pour into tubes or plates and test for sterility by incubation. The agar should be at 55°C. when the plasma is added. (3) The incubator temperature should be 35° C. to 36° C. (4) A dish of water should be kept alongside the cultures in the incubator.

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**The Transmissibility of Herpes Zoster to the Rabbit.**

*A. Luger and W. Lauda, Ztschr. f. Hyg. u. Infektionskrankh., 94:206, Berlin, Dec. 2, 1921.*

Inoculation experiments with herpes zoster material produced, in contrast to the typical injection reaction of herpes febrilis, no characteristic reaction on the cornea of the rabbit, as revealed by inoculation experiments of Löwenstein and Baum. On account of this contradictory behavior of herpes zoster and herpes febrilis, new transmission experiments were recently performed. The contents of herpes vesicles, blood-serum and cerebrospinal fluid were employed as inoculation material. The inoculation was performed partly through corneal infection by means of scarification of the cornea, and partly through intravenous injections. Corneal inoculation with the contents of herpetic vesicles was performed in 7 cases. In 1 case it was transmitted to the eyes of a guinea-pig. The data reveal that in no case did a characteristic macroscopical reaction result from the inoculation of the contents of herpetic vesicles. This behavior offers a possibility for distinguishing these 2 diseases by means of experiments. The cornea inoculated with herpes zoster is not immune against a recent inoculation with herpes febrilis. In contradistinction to herpes febrilis, it is not possible to produce a general infection with herpes zoster in the rabbit by corneal or intravenous injection of the vesicular contents, cerebellar fluid or serum of the patient. As regards the histologic changes, only the nuclear changes in the zoster vesicle of the skin described by Lipschütz as zoster vesicles could be observed, but not the changes of the cornea of the rabbit injected with zoster. The nuclear changes of the efflorescence of the skin are in accordance with analogous findings in herpes febrilis keratitis to be considered as degenerative changes, in contradiction to the chlamydozoic origin, suggested by Lipschütz. The microscopical picture of the cornea inoculated with zoster is characterized by the appearance of edema, giant-cells, cystic degeneration, intra-epithelial and subepithelial infiltration.

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**The Clinical Picture of Experimental Herpetic Genenar Infection of the Rabbit.**

*A. Luger, E. Lauda and E. Silberstern, Ztschr. f. Hyg. u. Infektionskrankh., 94:200, Berlin, Dec. 2, 1921.*

The possibility of transmission of herpes febrilis to the cornea of rabbits and guinea-pigs with consequent herpetic keratitis may be considered proved. In the animals infected with herpes, a series of symptoms appearing in 2 forms could be observed: attacks of paroxysmal convulsions, of short duration were often followed by an apparently

complete well-being. They were mainly tetanic cramps of the entire musculature of the body, particularly of the extensor. This stage usually lasts for thirty minutes. Then an opisthotonus and trismus develop, the animals recover, but a few days later a new attack finally proves fatal. The protracted attacks should be distinguished from these spasms. Tonic colonic twitchings and convulsions, and slight trismus are still present, the animals have symptoms of a severe general disease, have lost their appetite and exhibit manege movements. Between these 2 forms there are numerous intermediate forms.

The animal experiments demonstrate that animals injected with the contents of the vesicles present more general symptoms of the type of protracted attacks, while animals injected with the cerebromedullary substance become affected with the type of short attacks. No salivation could be observed, but fractures of the spine and also remissions of temperature were observed in younger animals. Pathologico-anatomic microscopical examinations of the internal organs of the central nervous system, and also the blood picture, have hitherto failed to reveal anything characteristic. A typical injection keratitis was produced by the injection of material from animals who had died of general symptoms; this fact proves that the general symptoms are due to the herptic infection.

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**Cultivation of the Causative Agent of Measles and Protective Inoculation with Living Organisms.**

*Rudolf Degkwitz, Monatschr. f. Kinderhilk., 22:186, Berlin, Nov., 1921.*

Degkwitz states, without giving details, that he has succeeded in cultivating the causative agent of measles, which does not belong to the class of the bacteria, from nasal and pharyngeal secretions. The cultures were bacteriologically sterile. Children who had never had measles, who were inoculated with these cultures, did not become ill with typical measles, but showed twelve or fifteen days later, rhinitis and slight elevation of temperature (up to 37.8°C.), of at the most seventy-two hours' duration. When exposed, several weeks or months later, to massive measles infection, they remained immune.

The organisms were cultivated on specific media, enriched by the addition of human protein, and inoculations through several generations were successfully carried out. The details of the study the author will publish when he has finished his experiments which are directed through growth on media of animal protein to laying the foundation of the manufacture of vaccine on a large scale. Only vaccination of young children seriously menaced by the danger of measles would offer a means of reducing the number of deaths from measles.

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**Studies upon Experimental Measles I. The Effects of the Virus of Measles upon the Guinea-Pig.**

*Charles W. Duval and Rigney D'Aunoy, J. Exper. Med., 35:257, Feb., 1922.*

The object of these experiments was the determination of the possibility of transmission of measles virus from man to the guinea-pig. They find that guinea-pigs react to intracardiac injections of defibri-

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nated blood cases of human measles with a rise in temperature and decrease in the number of leukocytes, when the blood is taken during the eruptive stage of the disease. Guinea-pigs which react and recover are not susceptible to reinoculation. Furthermore, propagation of the virus is obtained by passage of the blood from infected to normal guinea-pigs, although a typical exanthem is not produced.

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**A Study of the Virulence of Meningococci for Man and of Human Susceptibility to Meningococcic Infection.**

*George D. Heist, Solomon Solis-Cohen and Myer Solis-Cohen, J. Immunol., 7:1, Jan., 1922.*

It has been definitely proved that in the case of the pneumococcus, meningococcus and diphtheria bacillus, animal susceptibility and bacterial virulence may be clearly demonstrated and, to some extent, measured *in vitro* by cultivating the bacteria in whole, coagulable blood. This series of experiments was undertaken to find out whether, if meningococci from the spinal fluid of cases of meningitis and those from the throats of carriers were grown under like conditions in whole, coagulable human blood, some light would be thrown on their comparative virulence; and whether, if a strain of meningococci from a severe case of meningitis were grown in the blood of different individuals, some light would be thrown on the comparative susceptibility of men to meningococci infection. Experiments were carried out to test the effect of colon bacilli and Streptococcus hemolyticus in whole blood. A table shows that there were sufficient streptococci present to produce vigorous growth in the blood of all but 2 of the 15 men tested, even in a 1:100 dilution; while another table shows that the colon bacilli grew in only one of the entire lot of capillary tubes. These experiments further proved a certain correlation between the ability of bacteria to grow in whole, coagulable blood of man and their virulence for man. Therefore, the same method was applied to the experiments on meningococci.

The strains were isolated from the spinal fluid of 2 meningitis cases. They were grown on beef infusion agar plus 7% horse serum and 1% dextrose. The reaction was finally adjusted to pH 7.4. The method adopted by the United States Army for the detection of meningococcus carriers was followed, excepting that serum-dextrose-agar replaced blood agar. Only strains completely agglutinated by polyvalent antimeningococcus serum, 1:100, with clearing of the supernatant fluid after eighteen hours at 55°C. and having the cultural and morphological characteristics of meningococcus, were used. Cultures were ruled out if there was any trace in the controls of agglutination with normal horse serum, 1:50, or with salt solution. Normal and para serums were used in typing. Distinct agglutination by 1 serum alone was accepted as sufficient evidence that the strain belonged to that type. The use of a young culture of meningococci for tests with whole blood is a vital point. A series of tables give the results of the experiments on the meningococci isolated from the 2 cases and from carriers. The results show that these freshly isolated meningococci cultured in capillary tubes of the whole, coagulable blood of normal men, are found to possess an ability to grow rapidly in that media. This ability is not possessed by the majority of strains of meningococci freshly isolated from the throats

of carriers. There is a correlation between the ability of meningococci to grow rapidly in whole, coagulable blood, and their virulence for the species from which the blood was taken. Even the throat strains from the meningitis patients were less virulent than those from the spinal fluid. Certain carrier strains grow better in whole, coagulable human blood than do others. The writers conclude that they are the most virulent for man. The majority of carrier strains are relatively low in virulence or nonvirulence. The fact that the whole, coagulable blood of most normal men will permit the rapid growth of spinal-fluid strains indicates that most men are susceptible to the attacks of meningococci that have passed through the human nervous system. The blood of but one among many normal men permits the rapid growth of carrier strains. This minority is more likely to develop meningitis after exposure to a carrier. It is probably among this group that most of the cases of meningitis occur.

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**A Study of Two Distinct Strains of Streptococcus Isolated from the Same Heart-Valve Lesion.**

*Katharine M. Howell, J. Infect. Dis., 30:299, March, 1922.*

From the same aortic lesion in a case of chronic vegetative valvular endocarditis, 2 strains of streptococci were isolated, one a typical *Streptococcus hemolyticus*, the other a typical *Streptococcus viridans*. On the basis of sugar reactions the hemolytic organism was classified as belonging to the *Streptococcus pyogenes* group, the nonhemolytic strain as belonging to the *Streptococcus salivarius* group. The two strains differed in their serologic reactions as well as in their reactions on blood and sugar mediums, and it was evident that parasitic existence in the same lesion had not acted in such a manner as to cause similarity of biologic properties. The characters of each organism and the differences between the two have remained fixed and constant through a period of two years of artificial cultivation. When first isolated the hemolytic streptococcus was much more highly virulent than the other strain, and had the unusual property of agglutinating rather than hemolyzing red blood corpuscles when grown in fluid mediums. The latter property and the virulence were both lost under cultivation. The viridans strain studied over a period of two years does not support the view that *Streptococcus viridans* gives rise to hemolytic descendants in each successive replating, or to the view that viridans colonies may develop from the hemolytic variety as the virulence of the latter decreases.

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**The Cytobacteriologic Examination of the Pus of External Tuberculous Lesions.**

*M. Mozer, Méd. infantile, 28:1, Paris, Jan., 1922.*

It is usually difficult to demonstrate tubercle bacilli in the pus of cold abscesses and other external lesions. If the inoculation test is resorted to, the diagnosis will require three or four weeks. For the uninfected pus of closed abscesses, the following method is very satisfactory: To a volume of the suspected pus are added 3 parts 0.1 soda solution and 5 parts distilled water. The mixture is gently warmed until the pus is fully dissolved. If the pus is composed mostly of poly-

nuclear cells, the mixture will be very viscid or jelly-like. When solution is complete, 10 more parts of water are added, drop by drop, the liquid being well agitated. When it is cooled, 2 parts of 50% alcohol are added. The alcohol lowers the density of the liquid sufficiently to permit the bacilli to accumulate in the bottom of the centrifuge tube. The liquid should be centrifugated for twenty minutes. The sediment should be spread with great care, the slide being inclined at 15° and gently moved to and fro until a thin, homogeneous film remains on the slide. Search should not be abandoned under fifteen minutes. It is practically impossible to find tubercle bacilli in open and infected lesions.

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**The Differentiation of Acid-Fast Bacteria by Examinations of the Eye.**

*Arthur Seitz, Ztschr. f. Immunitätsf. u. exper. Ther., 33:431, Jena, Dec. 30, 1921.*

Seitz carried out experiments on the eyes of rabbits and guinea-pigs to determine whether differential diagnosis of the various acid-fast bacteria can be effected by inoculating the anterior chamber of the eye. For this purpose he utilized tuberculous tissue (caseous guinea-pig glands), pure cultures of *typus humanus*, *typus bovinus*, Friedmann's turtle bacillus, and Piorkowski's chelonin, as well as saprophytic acid-fast forms from milk and timothy-grass: (1) Sharp differentiation was unobtainable. (2) Acid-fast organisms nonpathogenic in man may at times give rise to changes in the iris which are indistinguishable clinically, anatomically or pathologically from true tuberculous processes. (3) Reinoculation from eye to eye in the rabbit produced no, or hardly any, appreciable increase in virulence in the cases under consideration. (4) Bovine tubercle bacilli are not distinguished from other forms; the only difference is that they finally induce generalized tuberculosis in rabbits inoculated in the eye.

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**Comparative Investigations Concerning the Extractability of Various Acid-Fast Bacilli by Means of Ether-Acetone Mixtures**

*W. Pfannenstiel, Ztschr. f. Hyg. u. Infektionskrankh., 95:87, Berlin, Jan. 17, 1922.*

It is impossible to annul the acid-fastness of the so-called acid-fast bacteria by mere extraction with fat-solvent fluids, such as chloroform, ether, xylol, acetone. It is necessary first to render the tubercle bacilli completely accessible to the solvents by boiling, by strong acids or alkalies, or by mechanical methods. The wax derived from the tubercle bacilli, which is obtained by distilling the solvent, shows the same tinctorial behavior as beeswax; it is acid-fast and alcohol-fast with respect to Ziehl's method (being accessible to staining only after heating); lecithin is dissolved in this stain, but can be stained by Gram's method. Pfannenstiel extracted 21 cultures of 9 different acid-fast races with ether and acetone mixtures under exact conditions for the purpose of determining (1) the quantity of the extracted liquid substances, (2) the acid-fastness of the extracts thus obtained, (3) the acid-fastness of the bacilli and the extraction.

Friedmann's turtle tubercle bacillus and Moeller's timothy bacillus constantly yielded a small quantity of extract, whereas the bacilli of frog and chicken tuberculosis produced large quantities. In the case of the genuine tubercle bacilli (*typus humanus* and *bovinus*) and also of the butter bacillus (with or without passage through warm-blooded animals), the quantities produced were very variable.

The acid-fastness of the lipid extract is complete in the case of the genuine tubercle bacilli, the transition strains of the turtle tubercle bacillus and Moeller's timothy bacillus; it is incomplete in the case of the butter bacillus and the bacillus of frog tuberculosis; the acid-fastness of the extract of the bacillus of chicken tuberculosis is not microscopically visible at all, but only under the microscope in small flakes. In the case of the genuine tubercle bacillus, the butter bacillus (after long-continued passage through warm-blooded animals), and the bacillus of chicken tuberculosis, the bodies of the bacilli did not show any perceptible decrease of the acid-fastness after the completion of the extraction. All the other races showed a slight and variable decrease of the acid-fastness. These facts show that the quantity of lipid extractive substances is variable, that these substances are differently distributed in the bodies of the bacilli, and that their extractability is modified by changes in the mode of living (passage of saprophytes through animal bodies). The acid-fastness cannot be altogether dependent on the quantity of waxy substances soluble in ether and acetone, because there is no parallelism between the degree of the extractability and the decrease of the acid-fastness. Apparently physicochemical differences in the plasmatic structure play a part in this. The variations of the physicochemical structure appear to have their counterpart in corresponding variations of the pathogenicity. It is more difficult to deprive the pathogenic races of their acid-fast property than the saprophytic races.

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**The Length of Life of Turtle and Trumpet Bacilli in Guinea-Pigs, and Their Cultural and Biologic Characteristics in Passage through Animals.**

*Masaaki Koike, Ztschr. f. Hyg. u. Infektionskrankh., 94:444, Berlin, Dec. 2, 1921.*

Through observation of patients and through animal experiments it has been established that only the presence of a focus with living tubercle bacilli renders a successful therapeutic treatment possible. The various characteristics of Friedmann's turtle bacillus were studied in a series of experiments to ascertain: (1) the duration of life of turtle and trumpet bacilli in warm-blooded animals; (2) the morphologic and cultural characteristics of turtle and trumpet bacilli following passage through warm-blooded animals; and (3) the biologic character, especially the virulence, of the bacilli after prolonged stay in the bodies of warm-blooded animals. Cultures of Friedmann's bacilli from two to four weeks old, which had been kept in a temperature of 28°C., were diluted and injected subcutaneously, intraperitoneally and intramuscularly into guinea-pigs. The guinea-pigs were later killed and cultures taken from the points of injection and planted in Lubenau's nutritive egg-glycerin-agar medium. On the subcutaneous point of injection, bacilli were found microscopically, forty days after injection, and cul-

turally thirty-five days after injection. In intramuscular injections it was possible to observe bacilli both microscopically and culturally on the fifty-fourth day following the injection; in cases of intraperitoneal injection, on the one hundred and twelfth day. Bacilli were cultured from a peritoneal abscess on the fifty-fifth day following the intraperitoneal inoculation. It was not possible to produce, in guinea-pigs or mice, symptoms by means of inhalation of Friedmann's bacilli, not even when great quantities of the bacilli were employed. In cases of cutaneous inoculation it was possible to culture Friedmann's turtle bacilli from the deeper layers of the skin, on the fourth day following the inoculation; the bacilli were observed microscopically on the third day.

When Jakobitz and Kaiser examined a wind instrument which had been used by a tuberculous musician, they found numerous acid-fast bacilli, but similar bacilli were also found in other instruments which had not been used by the tuberculous individual. These so-called trumpet bacilli belong, according to Lange's examinations, to the same species of bacteria as turtle and frog tubercle bacilli. The examinations showed that when from 6 to 12 mg. trumpet bacilli were injected subcutaneously, bacteria were observed microscopically forty-three days after the injection and culturally thirty days after the injection. When injections were performed intramuscularly, the microscopic and cultural demonstration of bacteria was possible as late as the twenty-seventh day following the injection, and in the case of intraperitoneal injections, on the one hundred and eleventh day after the inoculation. The inhalation experiments on guinea-pigs and mice gave totally negative results. Increase of the doses lengthens the life of the bacteria. The injection experiments with tortoise and trumpet bacilli revealed only quantitative differences. In regard to the morphologic and cultural character of the turtle and trumpet bacilli, experiments proved that after a longer stay in warm-blooded animals, there was never a morphologic difference between the inoculated culture and the original strain; culturally it was observed that the inoculated trumpet bacilli, as well as the inoculated turtle bacilli, grew better at a temperature of 28°C. than of 37°. In many instances the bacilli failed to grow in the temperature of 37°C. At a temperature of 28°C., the growth of the trumpet bacilli was somewhat less profuse than that of the turtle bacilli. Finally, experiments were also made as to the biologic character, especially the virulence of turtle and trumpet bacilli in warm-blooded animals. The experiments revealed that an increase of the virulence is not caused by passage through animals. As only a few experiments were performed, final conclusions in this respect cannot be drawn. Future reports will reveal the results of experiments concerning the difference in virulence between quantitatively graded subcutaneous, intra-ocular and inhalation infections..

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A Tuberculosis Disease in Salt-Water Fish (Halibut) Associated with the Presence of an Acid-Fast Tubercle-Like Bacillus.

P. L. Sutherland, *J. Path. & Bacteriol.*, 25:31, Edinburgh, Jan., 1922.

On examination the liver and spleen of a tuberculous halibut were found to contain numerous grayish-white nodules. Projecting under the peritoneal covering of the roe were many whitish tubercles. A

cross-section of the organ showed small round areas of disease about  $\frac{1}{4}$  in. in diameter. Transverse sections of the subcutaneous tissue and muscle showed a diseased condition on both the dorsal and ventral aspect. This tissue was soft, almost gelatinous, and of a light-yellowish color. The stomach and intestines were apparently normal. Microscopic examination of the affected tissues showed many bacilli, suggesting the condition of tuberculosis. The bacilli were slender, distinctly acid-fast rods, varying considerably in length and occurring singly, or in pairs, lying parallel and in small groups. Morphologically the organisms were practically indistinguishable from the bacilli of mammalian tuberculosis. In sections of tissue stained by the Ziehl-Neelsen method the bacilli retained the stain in spite of the treatment with alcohol to which they were subjected in the process of dehydration. They were scattered generally throughout the granulomatous tissue, especially abundant among the central cells and the necrosed portions of the larger tubercles; in some cases the bacilli were distinctly intercellular. Acid-fast bacilli occurred in broth incubated at 20° C., large masses of bacilli were found on examination of the deposit which formed at the bottoms of the tubes. However, contamination of the cultures with other more rapidly growing organisms prevented the obtaining of pure cultures. A reproduction of the disease could not be effected in either guinea-pigs or frogs. The lesions in the halibut show that salt-water fish like fresh-water fish, frogs, and other cold-water vertebrates, suffer from diseases which more or less resemble tuberculosis and are caused by acid-fast tubercle-like bacilli.

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The Production of CO<sub>2</sub> by the Typhoid Bacillus and the Mechanism of the Russell Double Sugar Tube. II. Fermentation or Respiration. Phenol Red as an Indicator.

Henry J. Nichols and Cyrus B. Wood, *J. Infect. Dis.*, 30:320, March, 1922.

The CO<sub>2</sub> produced by the typhoid bacillus on the Russell double sugar medium is probably fermentative as well as respiratory. Phenol red is the best indicator as it shows both the acid change in the butt and the alkaline change in the slant. A pink phenol red Russell sugar tube, pH 7.2 to 7.4, twenty-four hours after inoculation shows a yellow butt, pH 6.8, and red slant, pH 7.8. In forty-eight hours the changes are more marked, and after a week the whole tube becomes red. In sealed tubes both the butt and the slant become yellow, or acid, and remain so.

The preparation of the medium is carried out as follows: Make extract agar (3% shred agar); clear; add 1% lactose and 0.1% glucose and 5% of a 0.02% watery solution of phenol red. Correct reaction to pH of 7.2 to 7.4 hot. Tube, sterilize and slant so that there will be a deep butt and a long slant. The final reaction cold will be 7.2 to 7.4 as the tendency to a more alkaline reaction in cooling is overcome by a slight acidity developed in sterilization.

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Definition of Experimental Typhus Fever in Guinea-Pigs.

Peter K. Ollitsky, *J. A. M. A.*, 78:571, Feb. 25, 1922.

The object of this paper is to draw attention to the conditions  
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necessary to establish experimental typhus fever in guinea-pigs; to indicate the nonspecific or pseudo reactions which should be considered as possibilities in the determination of each of these criteria, and finally to show that no interpretation of an experiment can be made unless all the requirements are met and the nonspecific or pseudo reactions are considered. Experimental typhus fever presents constantly and regularly certain manifestations which, taken together, stamp it unmistakably as a typical disease. These manifestations in the guinea-pig consist of a characteristic febrile reaction, of indefinite transmissibility from animal to animal, particular histologic changes in various organs, but mainly in the brain, absence of bacteria cultivable in any aërobic or anaërobic medium whatever, and finally, immunity, determined by cross-immunity tests, to materials carrying known typhus virus. Besides these manifestations, what have been termed nonspecific or pseudo reactions in the guinea-pig, simulating particular manifestations of the action of true typhus virus, have been described. The latter reaction can be induced by a variety of substances, and failure to recognize this fact may lead to erroneous interpretation of inoculation experiments in guinea-pigs in studies on the etiology of typhus fever. To establish immunity, experiments should always be repeated, the possibility should be considered of the presence in cultures of substances found in typhus-infected tissues which are not living, multiplying agents, but which may occasionally induce immunity, and finally cross immunity tests should invariably be performed.

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**Experimental Studies on the Etiology of Typhus Fever.  
II. Survival of the Virus in Aërobic and Anaërobic Culture Media.**

Peter K. Olitsky, *J. Exper. Med.*, 35:115, Feb., 1922.

Olitsky tested the virus of typhus fever experimentally to study the nature of any inciting agent which might be found therein. The virus does not survive at 37° C. in anaërobic media for as long a period as in the same media under aërobic conditions. The dead virus fails to induce the experimental disease or immunity to further injections. In Smith-Noguchi medium the typhus virus dies after twenty-four hours, showing that it is not identical with the *Bacillus typhi exanthematici* of Plotz.

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**Experimental Studies on the Etiology of Typhus Fever. III.  
Filtration Experiments.**

Peter K. Olitsky, *J. Exper. Med.*, 35:121, Feb., 1922.

The typhus virus in the tissues of the guinea-pig during the height of reaction to the experimental disease does not lose its infecting power when the cells of the brain or of the spleen are disintegrated by freezing, crushing, and grinding, in various ways. The virus after such treatment is as actively infective as in the same tissue not subjected to the disintegrating influences. The possibility therefore exists that there may be an extracellular condition of the typhus virus. Attempts to filter it through Berkefeld filters all resulted in failure.

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**Observations on Castellani's Vibriotrix Zeylanica.**

*Igino Iscomo, Riforma med., 33:32, Naples, Jan. 9, 1922.*

In the bacteriologic study of the feces of dysenteric patients, one always finds an organism isolated for the first time by Castellani, who called it *Vibriotrix zeylanica*. Its polymorphism renders it doubtful whether it should be classified with bacteria or with higher fungus forms. When the various colonies of organisms contained in the evacuation of dysenteric patients are transferred from simple or glucose agar, spread out in Petri dishes, in sugared broths, and a biologic study made, certain colonies are observed, very similar to those of the dysentery bacteria, which produce upon the surface of the liquids a greyish and coarsely granulated pellicle. This is made up of the *Vibriotrix zeylanica*. Colored with common anilin dyes, or observed in hanging drops, the vibriotrix presents itself under the microscope simultaneously in the form of a bacillus, a vibrio, spirillum, or a pseudospirillum.

The vibriotrix is mobile and Gram negative; it does not liquefy either gelatin or serum. It grows rapidly on simple or glucose agar, in the form of a thin, greyish-white film. It does not produce gas in the glucose, in any of the series of sugars, or in glycerin. It renders milk alkaline and decomposes only glycerin and arabinose, with the production of acid alone. Glucose, maltose, saccharose, dulcite, inulin, galactose, lactose, dextrin and mannite, into which the organism has been planted present an alkaline reaction even after twelve days, and their surfaces show the pellicle described above. The broth becomes uniformly turbid, and the indol reaction is negative. The blood-serum of dysenteric patients does not agglutinate this organism, even in high concentration. Even when the pathogenic properties of the organism itself are left out of consideration, it is probable that, living in symbiosis with the etiologic agents of dysentery, it plays a part of great importance in the pathogenetic mechanism of dysenteric ulcer.

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**The Theory of Disinfection in the Light of the Meyer-Overton Lipoid Theory.**

*P. G. F. Vermast, Biochem. Ztschr., 125:106, Berlin, Dec. 8, 1921.*

According to the Meyer-Overton theory the permeability of a substance into the living cell is first of all dependent upon its solubility in fat or fatlike substances. For the rapidity of the progress of osmosis, the relative solubility of a certain combination in the lipoid phase is decisive on the one hand, and on the other hand its solubility in the surrounding medium as a second phase; the substance penetrates the cell the more easily, the greater the quotient obtained by dividing lipoid by water. Overton, however, called attention to the fact that the size of the quotient and also the absolute lipoid solubility must not fall below a certain limit. Waterman showed that the absolute solubility in the surrounding medium (water) has a minimum limit, below which a disinfecting effect is not seen.

From chemicophysic observations of the disinfecting effect of acid disinfectants the conclusion is drawn that the power of disinfection of any particular substances with one and the same total concentration must rise or fall with their degree of dissociation. Two methods are

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generally used for the valuation of disinfectants: In one, the bacterial strain serving as test object is suspended in aqueous solutions containing increasing amounts of the disinfectant; after subsequent inoculation it is determined in what concentration in a specified time and at a definite temperature bacteria are killed; this method is not always applicable. In the other method, the disinfectant is added in increasing amounts to a series of culture tubes containing appropriate nutrient media, the various tubes are inoculated and kept for varying methods of time at the proper incubation temperature and it is determined at what concentration the tube contents remain sterile. There are also objections to this method.

The nutrient media contain salts which affect the hydrogen-ion concentration (neutral reaction) controlling the artificial nutrient media partly as primary phosphates and bicarbonate. Such mixtures of weak acids with their alkaline salts and also weak bases with their chlorides, sulphates, etc., are designated as reaction regulators or buffers; they can stabilize the hydrogen-ion concentration of a certain mass and prepare more or less great reservoirs for the subsequent delivery for hydrogen or hydroxyl ions, which are at first potentially combined but are liberated by disturbances of equilibrium, and also vice versa, they may combine in case they appear free in the solution. In such regulator or buffer solutions respectively, a hardly demonstrable change of pH results from the addition of small amounts of very weak and slightly dissociated acids. Experiments conducted with the weak organic acids, as salicylic and benzoic acids, showed that the amounts of these acids which are supposed to produce disinfection must increase with the amount of the regulator capacity of the medium; this holds true in various nutrient media of like pH.

A series of culture tubes were prepared with a definite amount of medium containing increasing quantities of the disinfectant; to each tube was added with 3 drops colon bacillus emulsion; only tubes made of Jena glass were used, which can be sterilized when moist; they were of uniform diameter so that they could be used for immediate colorimetric determination. The hydrogen-ions were also determined colorimetrically; the Sörensen method of colorimetry was found the best, and as the comparative fluid with known hydrogen-ion concentrations, the citrate tenth-normal and citrate tenth-normal hydrochloric acid mixtures, recommended by Sörensen, were used. Methyl-red was used as indicator, 3 drops to 10 c.c. It was important to keep all solutions free of CO<sub>2</sub>. The available color difference with methyl-red varied from pH 4.2-6.3. The investigations showed that very slight changes of the hydrogen-ion concentration may result, in fairly marked variations in the total concentration of the benzoic acid anions, in producing disinfection. In this also the significance of the hydrogen-ion concentration of such disinfection experiments is noticeable; all the experiments also gave evidence that with an acid reaction not the total concentration of the benzoic acid anions, but the concentration of the unsplit benzoic acid molecules alone is responsible for the cellular death; as soon as the latter has reached a certain value the disinfecting action always appears; this finding corresponds with the theory of Meyer-Overton.

The experiments show that in neutral and acid media disinfection always occurred with like concentration of the benzoic acid, in spite of the fact that the total amount of the benzoic acid radical and hydrogen-

ion concentration were subjected to marked variations. Organic acids, like benzoic and salicylic acids, penetrate the living cell according to the laws of the separation quotient, according to their electrolytic dissociation in neutral and acid media. This action is explainable by the Meyer-Overton lipoid theory. Variations from the lipoid theory were found in alkaline media: with increasing hydroxyl-ion concentration, the disinfecting action always appeared. Why this should be so has not yet been satisfactorily explained. To determine the value of the disinfecting power it is necessary to consider the concentration of the unsplit molecules and the reaction of the medium, with which the disinfecting action appears in a definite time. The closer examination of various organic acids with the aid of the results thus obtained can determine whether the disinfection value of organic acids runs parallel with the size of the division quotients of their unsplit molecules in the lipoid-water system. The salts of organic acids as such possess no disinfecting capacity in nonalkaline media; it is doubtful whether they possess such in alkaline media.

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**A Holotrichous Ciliate Pathogenic to Theobaldia Annulata Schrank.**

*W. P. MacArthur, J. Roy. Army M. Corps, 38:83, Feb., 1922.*

The holotrichous ciliate of the suborder Hymenostoma has thus far been found in the blood of *Theobaldia annulata*. The body varies in shape from elongate oval to broad oval, and is longitudinally striated. There is much difference in size, but most of the forms vary in length from 25 to 41 microns. The maximum breadth of a well-grown individual lies between 15 and 25 microns. Considerable variations in size and shape are noted; the rapidly swimming forms are relatively long and narrow and are concave ventrally and convex dorsally; the more slowly moving individuals are shorter and broader, and more or less barrel-shaped. The smaller individuals show a long caudal cilium; this tail-like structure is present but much shorter in the forms intermediate in size, and is absent in the largest ciliates. The nucleus is spherical and in unfixed specimens usually measures 9 to 12 microns. The micronucleus usually lies close to the nucleus, sometimes indenting its margin, and is usually 1.8 to 3 microns in diameter. The cytostome is placed anterolaterally, and varies from 3.6 to 9 microns in length, and from 1.8 to 4.5 microns in breadth. The cytosome is surrounded by circumoral cilia, which are longer in the young individuals. The endoplasm is granular and usually contains 1 to 27 food vacuoles. There is no anus, food remnants being extruded through the cortex. When the exoskeleton of the infected larva is ruptured, ciliates dash through the breach and swim about most actively, tending to slow down later. Reproduction takes place by binary fission. The product resembled that of ordinary binary fission. Infection of the larvae probably occurs by ingestion of small ciliates; these might readily pass through the gut wall into the blood cavity and spread over all the body. Different stages of this ciliate show various transitions that make it appear to cut across characters on which a number of different genera have been founded; possibly *Uronema*, *Cyclidium*, *Pleuronema* and *Glaucocoma* may all belong to the same genus.

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**The Incidence of a Leptospira in the Kidneys and of Parasites in the Intestines of 100 Wild Rats Examined in England.**

*A. C. Stevenson, Am. J. Trop. Med., 2:77, Jan., 1922.*

A great deal of work along this line has demonstrated the Leptospira icterohaemorrhagiae in the kidneys of wild rats. It was supposed that the seasonal incidence was of importance. However, Blanc points out that possibly locality is more important than season. Stevenson examined 50 rats between Feb. 2 and March 15 and another 50 between May 2 and June 2. Giemsa-stained smears and Levaditi-stained sections of the kidney were the methods used to demonstrate the parasites. Of the first batch of 50, 12 were found infected; of the second batch, 18 were infected. All the positive rats except 1 came from the London district. In 52 of these 100 cases the urine was examined by the dark-background method and 18 were found to be positive, although leptospira was only demonstrated in the urine of 9. In the smears, the organism was found singly and in coil masses both large and small. The organism was also found blocking the lumen of the kidneys. From these experiments the writer concludes that: (1) There may be a high incidence of leptospira, probably Leptospira icterohaemorrhagiae, in rats in an area where the disease is practically unknown. The high rate of incidence shown by the Japanese was correlated with the area being one where the disease was endemic. (2) It is very unlikely that the incidence is greater during the winter months. In the second batch of cases in early summer the number of rats affected was 50% greater than in the later winter months.

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(1d—200)

**Observations on the Biologic Characters of the Leptospira Icterohæmorrhagiæ.**

*A. Stanley Griffith, J. State Med., 30:70, London, Feb., 1922.*

In cultivating the Leptospira ictorhaemorrhagiae, the medium which gave the most consistently good results was semigelatinous bovine serum, to which had been added a small quantity of fresh citrated blood of a normal guinea-pig. The cultures have grown at 2 temperatures only, 37° and 25° C. The observed maximum duration of life of an individual culture of the spirochete is sixteen months. Only virulence tests have been made on the guinea-pig and the rat, with the Belgian strain of spirochete.

From the tests made on the guinea-pigs, it was found that they may sometimes possess a very high degree of natural immunity to the disease. The experiments made on the rat, show that it was resistant to the inoculation of spirochetes which are highly virulent to guinea-pigs. The spirochetes are not, however, all destroyed in the body of the rat but some may pass into the kidneys where they live and multiply and from which they are excreted with the urine. This excretion from the kidneys appeared to be intermittent, since the urine of the rat was not infective on one occasion, but was so on the next.

In view of the favorable reports of the Japanese observers, Inada and Ido, it was decided by the Medical Research Committee to supply a curative serum for the use of the British troops in France among whom cases of infectious jaundice had occurred. The immunization

of a horse was, therefore, begun on February 6, 1917. It died from embolism due to an intravenous injection of cultures. The second trial was successful and after ten months immunization occurred. During this time 33 immunizing doses had been given, the doses being gradually increased. The serum was not tested until 1919 owing to the loss of the virulent guinea-pig strain. It was finally tested, however, against a French strain of spirochete, just one year after the serum had been withdrawn. While small doses of the serum prolonged the life of the guinea-pig, it did not prevent the development of the disease. Some Japanese serum was also tested against the French strain of spirochete but while it also prolonged the life of the guinea-pig, it failed to prevent its death. These tests with the French strain against the Japanese and the author's horse sera show that the French, Belgian and Japanese strains of the spirochete are immunologically closely related.

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**Caulleryella Maligna N. Sp. Schizogregarina Pathogenic for Cellia Allopha of Lutz and Peryassu.**

*Alcides Godoy and Cesar Pinto, Brazil-med., 33:46, Rio de Janeiro, Jan. 28, 1922.*

In the course of study of the anopheline mosquito, Godoy and Pinto found in the intestines of larvae, both young and adult, of *Cellia allopha* an interesting schizogregarina presenting the characteristics of *Caulleryella Keilin* 1914. These anopheles larvae under examination were all destroyed by the infection of *Caulleryella maligna*, either dying in the focus contaminated by the schizogregarina, or reaching maturity, and then perishing in spite of attempts made to nourish them.

Later studies will discover what rôle this protozoan plays in the destruction of the anopheles. The intestinal lesions of the larvae of *Cellia allopha* caused by the intense parasitism of *Caulleryella maligna* fully account for the death not only of larvae, but also, and chiefly, of adults. A description of the dimensions and form of the *Caulleryella maligna* is given, with numerous illustrations. In material coming from larvae of *Cellia allopha* a curious phenomenon was observed in rounded forms of *Caulleryella maligna* at a temperature of 27° C. or less. After a certain period of time a fine pellicle appeared which was later completely expelled, after which an internal membrane was observed in the protozoan within which was an intense movement of small particles. This soon ceased whereupon a marked retraction of the endoplasm was noticed. It was impossible to interpret the meaning of this phenomenon.

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(1d—202)

(1d—202)

**Vital Staining of Treponema.**

*Paul Vigne and E. Pringault, Marseille-méd., 59:19, Jan. 1, 1922.*

After studying the attempts of various men in vital staining with treponema, Vigne and Pringault were led to use a solution of Chinese blue, 1/500 in physiological serum 7.5/1000. Their procedure is as follows:

A drop of the serous solution to be examined is mixed on the slide with a drop of the physiological solution of Chinese blue. This is placed on a very thin cover-slip and examined with the ultramicroscope. The

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spirilla are colored in red; cells, including leukocytes, and erythrocytes, are colored a faint blue. This double coloring is due to the phenomena of fluorescence. The treponema have lost neither their morphology nor their movements. Other flagellates, particularly *refrigens* and *Treponema dentium*, are found. The spirilla of balanitis also show the phenomena of fluorescence.

This procedure has, moreover, the advantage of not altering the simplicity in the employment of the ultramicroscope, or the necessitating of a single complicated fixation or coloring, and above all of preserving the essential characteristics of the treponema.

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### A New Method of Preparing Freezing Sections of Spirochetes.

*G. Steiner, Münch. med. Wchnschr., 69:121, Jan. 27, 1922.*

The material is fixed in formalin, washed for one hour in running water, and freezing sections are prepared 10-20 cm. thick. The sections are then allowed to remain for one or two minutes in a 10% alcohol solution of mastic (alcohol 96%) and washed twice with distilled water. Then they are allowed to remain for twenty-four hours at 37° C. in a 0.1% solution of silver nitrate. Washing for a short time, with hot distilled water, follows. The sections are placed for ten minutes in a milky solution of mastic (1 c.c. of the above-mentioned alcoholic mastic solution, 10 c.c. 96% alcohol, and 20-30 c.c. distilled water). After brief rinsing with distilled water, the sections are allowed to remain for four or five hours in a 5% solution of hydrochinon. After that they are thoroughly washed with distilled water.

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### Two Recent Improvements in the Staining of Spirochetes in Nervous Tissue.

*George S. Stevenson, Arch. Neurol. & Psychiat., 7:349, March, 1922.*

The failure of foreign investigators to obtain satisfactorily constant results with existing silver-impregnation methods in nerve tissue led Jahnel to devise his method. Stevenson's experience with this method has been very satisfactory. The technic, while requiring a long time, offers no difficulties if the directions are faithfully followed. With a subdued yellow to yellowish-brown background the spirochetes stand out in marked contrast. The staining of nerve fibers is so suppressed as to eliminate any confusion with the spirochetes. Granulation, fraying and precipitate are negligible. Old chemicals must never be used. No modification of the original method has been found necessary. Fixation should be complete; most beautiful preparations were obtained from tissues that had been in formaldehyd for ten years. The author's improved method is as follows: (1) Fix completely in 10% formaldehyd solution, U.S.P., pieces from 5-7 mm. thick. (2) Embed in paraffin without washing in water. (3) Cut from 5-12 micron sections and mount on specially prepared cover-slips with minimum albumin fixative ( $\frac{3}{4}$  in. No. 1 cover-slips, cleansed thoroughly and dried in an incubator for twelve hours). (4) Remove the paraffin

(warm over a flame, wash with xylol, descending alcohols and water). (5) Immerse section in 1% uranium nitrate (distilled water) five to eight minutes. (6) Wash in distilled water one minute. (7) Rinse section and a clean cover-glass in fresh silver nitrate solution 2%; apply the rinsed cover-glass to the section so that they will adhere by capillary attraction, and put edge up against the side in a dark bottle containing  $\frac{1}{2}$  in. (1.27 cm.) of fresh 2% silver nitrate solution; cork tightly; incubate from thirty to sixty min. in the dark. (8) Separate the cover-slips and put section into the following reducer; (remove when yellowish to reddish brown): Mix 2% silver nitrate 3 c.c., warm 10% aqueous gelatin 5 c.c., warm glycerin 5 c.c.; with stirring, add warm 1.5% agar suspension, 5 c.c. (the agar suspension is made by mixing 1.5 gm. agar with 100 c.c. cold distilled water, heating slowly, and stirring constantly until it boils; continuing to boil until suspension is complete; to be kept on top of the paraffin oven); with stirring add a 5% aqueous hydroquinone solution 1-2 c.c. just before immersing sections. (9) Rinse the section in a 5% solution of sodium thiosulphate. (10) Rinse the section in distilled water. (11) Treat with ascending alcohols, xylol; mount in balsam.

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(1d—205)

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**A Simple Method of Detection of Spirochaeta Pallida.**

*J. Lenartowicz, Polska gas. lek., 1:44, Warsaw, Jan. 15, 1922.*

Conjointly with Potrzobowski the writer indicated a method of detecting *Spirochaeta pallida*, which consists in a fixation of the material to be investigated by 0.5-1% solutions of osmic acid and subsequent staining with Ziehl's fuchsin solution. As osmic acid is very expensive and difficult to procure, and does not keep well, the writer tried to replace it by a cheaper and more stable product. Undiluted formalin (40% formaldehyd) was found to be an excellent substitute.

The writer recommends the following method: (1) A clean object glass, free from fat, is placed over the mouth of a small bottle containing 30-50 c.c. of 40% formalin, so that it covers it. It is allowed to remain in that position for one-half or one minute. (2) The serum, which must be as pure as possible, is spread in a thin layer upon a portion of the object-glass which has been subjected to the action of formalin, by means of a platinum wire. (3) The covered object-glass is again subjected to the action of formalin vapors for one minute. (4) After the serum on the object-glass is dry, it is stained by immersing it for fifteen to thirty seconds into Ziehl's fuchsin solution. It is then rinsed with water and dried between blotting paper. It is examined under immersion without a cover-glass. The spirochetes are visible as unstained spots upon a red background, while bacteria and refractive spirilla are stained dark red. To obtain good preparations it is necessary that the layer of the serum be as thin as possible.

Correctly made preparations have a shining surface. While Giemsa's method does not render possible a distinct staining of the spirochetes, and Burri's method renders the examination very difficult on account of the dilution of the material, the method described produces distinct pictures revealing a comparatively high number of spirilla.

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**A Study of the Relation of Treponema Pallidum to Lymphoid Tissues in Experimental Syphilis.**

*Louise Pearce and Wade H. Brown, J. Exper. Med., 35:39, Jan., 1922.*

The problem was approached by a series of experiments designed to show the frequency, time, and extent of lymphatic dissemination of spirochetes from a primary focus of infection in the scrotum or testicle. The method employed consisted of the demonstration by animal inoculation, of *Treponema pallidum* in the lymph-nodes of infected rabbits. They found that a wide-spread dissemination of the organisms occurs by way of the lymphatics. Spirochetes were found in the lymph-nodes as early as two days after inoculation. It has further been showed that a syphilitic infection is sufficiently established in the rabbit within forty-eight hours after scrotal inoculation, and that a primary lesion is no longer necessary for its maintenance. Active treponemas survive in the lymph-nodes for a long time. The persistence of spirochetes in lymphoid tissue, irrespective of syphilitic lesions, is a characteristic feature of syphilis in the rabbit. The infection is primarily one of lymphoid tissue.

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**Venereal Spirochetosis in American Rabbits.**

*Hideyo Noguchi, J. Exper. Med., 35:391, March 1, 1922.*

Review of the foreign literature suggested the examination of American rabbits. Of 50 rabbits examined in June, 1921, from the Rockefeller Institute, 3 females and 2 males were found to have lesions of the vulva, prepuce, and perineum. One female rabbit, born at this Institute six years ago, has been kept as normal breeding stock, and has never been used for experimental work. Recently 6 females with similar lesions have been found among 20 rabbits just purchased. This condition runs a chronic course and is characterized by the presence of a spiral organism closely resembling *Treponema pallidum*. Rabbit spirochete has the same morphological features as *Treponema pallidum*; it is possibly a trifle thicker and longer than the average pallidum. In the lesion of one rabbit there were 2 types of spirochete, one of the variety described, the other, a somewhat coarser organism, closely resembling *Treponema calligyrum* found in a human condyloma, but a trifle thinner and longer. The histological reactions are similar to, but less cellular than, those occurring in typical primary syphilitic lesions. The disease is transmissible to normal rabbits, in which the usual papular lesions can be readily reproduced in the genitoperineal region. In the first passage the incubation period varied from twenty to eighty-eight days, subsequently one of the strains produced a lesion in twenty days on the second, and five days on the third passage. Monkeys failed to show any lesions within a period of four months after inoculation. In one instance transmission was accomplished through the mating of an infected female with a normal male. Wasserman reaction was uniformly negative in the 5 rabbits with spontaneous lesions and in 18 rabbits experimentally infected. Salvarsan had the same therapeutic effect on the lesions produced by the rabbit spirochete as on the experimental pallidum lesion of the rabbit. The organism belongs to the genus *Treponema*, and may be designated *Treponema cuniculi*.

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**The Cultivation and Biologic Characteristics of Spirochaeta Obermeieri (Recurrentis).**

*I. J. Kligler and O. H. Robertson, J. Exper. Med., 35:303, March 1, 1922.*

In attempts to cultivate the spirochetes of relapsing fever the Noguchi method was found the most satisfactory, but the results were inconstant and it seemed desirable to analyze more fully the factors in the growth requirements of these organisms. Ascitic fluid, horse or rabbit serum, was necessary for the growth. Inactivation of the serum was found to be unnecessary, and coagulation undesirable. The addition of kidney is not necessary. The physical condition of the medium seems to exert an important influence and the concentration of hydrogen ions in the medium is an important limiting factor in affecting the growth and viability. These fluids became progressively more alkaline on exposure to air. Growth is more rapid in undiluted serum, but the viability of the culture is greater in diluted serum. In media having a reaction below pH 7.0 or above pH 8.0 there was apparently no growth, while the maximum rate of multiplication occurred between pH 7.2 and 7.4. Spirochaeta obermeieri is a strict aërope, consequently to permit adequate aeration the oil layer should not exceed 1.5 cm. in height.

The organisms were cultivated consistently from the blood of infected mice and rats; the viability of cultures was maintained for periods of at least three to seven weeks; and successive subcultures were carried on by transplanting at intervals of two to four weeks.

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**Species of Hymenolepis as Human Parasites.**

*Asa C. Chandler, J. A. M. A., 78:636, Mar. 4, 1922.*

The genus Hymenolepis includes a large number of species of tapeworms. There seems to be little doubt that their primitive and typical life history involves an invertebrate as an intermediate host for the larval stage, which is a cysticercoid. The human species, *Hymenolepis nana*, has a life history similar to that of *Hymenolepis murina*, the common rat tape-worm, which usually develops without the intervention of any intermediate host. The question as to whether infestation can occur only by means of eggs acquired from human beings through such agencies as dirty hands, contaminated water, raw vegetables, flies, or internal auto-intoxication, or also by means of eggs ingested with the excreta of infected rats or mice, is one which cannot be determined until the identity or distinctness of the 2 species has been finally settled. The frequency of infestation with *Hymenolepis nana* varies greatly in different parts of the country. It is the most common parasite of human beings in the Southern states, and probably in most localities.

In the case of *Hymenolepis diminuta*, the human parasite is identical with that of rats. It is one of the commonest worms infesting rats. Human infestation occurs by the accidental swallowing of an intermediate host, as the larva of the meal moth or worm, found in corn-meal, breakfast cereals, potato chips or dried fruits eaten without cooking. As the records of only 35 cases are available, with wide

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geographic distribution, it seems certain that it is a parasite normally harbored by an animal other than man, and conveyed to the human host by an agency which is not commonly realized. It is possible that human infestation with other species may occasionally occur.

The effects produced are comparable to those produced by other tape-worms: abdominal pains, convulsions, epilepsy, insomnia, headache, dizziness and eosinophilia. Male fern is the drug most frequently employed in treatment. *Hymenolepis nana* infestations have a tendency to recur. *Hymenolepis diminuta* is very easily expelled by anthelmintics or by a cathartic. The reason for the nonoccurrence of other species of *hymenolepis* in man is not so much the inability of the worms to subsist in the human intestine as it is their failure to remain attached, and their consequent early expulsion.

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### A Note on Grappling Tail-Hooks in Anopheline Larvas.

*M. O. Tirunarayana Iyengar, Indian J. Med. Research, 9:630, Calcutta, Jan., 1922.*

Grappling tail-hooks are present in a large number of Indian anophelines. The posterior dorsal region of the anal segment has a set of 4 tufts of setae, a median pair and an outer pair. The median pair starts from either end of a transverse strip of chitin, and is anterior and dorsal to the outer pair. The outer tufts start from 2 curved beak-like plates of chitin on either side of the median line, and which in some cases may be fused at the base. These plates could be seen only when the setae were pulled out. The median tufts are of the feathered type and, when the larva is at rest, they are projected backward and upward from the tip of the anal segment. There are many more branches on the dorsal than on the ventral side. Grappling tail-hooks are found to be present quite characteristically in the following species: *subpictus* (Giles), *jamesi* (Theob.), *maculipalpis* (Giles), *maculatis* (Theob.), *minimum* (Theob.), *funestus* var. *listoni* (Liston), *stephensi* (Liston), *barbirostris* (v.d. Wulp), *hyrcanus* (Pallas) and *gigas* (Giles). When disturbed, the anopheline larvae hang by their tail-hooks to boulders or aquatic plants, and thus save themselves from being carried to the bottom of the stream, where they are exposed to danger from the pressure of the water and from fish. When attached to boulders, stones, or aquatic plants, the anopheline larvae can withstand strong currents of water.

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### Some Notes on Indian Calliphoninae.

*W. S. Patton, Indian J. Med. Research, 9:548, 555, 561, 570, Calcutta, Jan., 1922.*

*Lucilia argyricephala*, Macq. (*Serenissima* Fabr.) The common Indian bazaar green bottle, whose larvae occasionally cause cutaneous myiasis in animals, and *Lucilia cargii*, sp. nov., one of the common blow-flies of the Indian hill stations:

The egg of *Lucilia argyricephala* is smaller than that of *Chrysomyia bezziana*. When first laid it is creamy white but later becomes yellowish. From 380 to 460 eggs are usually laid in a mass. The larvae

hatch out in twenty-four to thirty-six hours. The mature larvas measure about  $\frac{1}{2}$  in. in length and are of a dirty white color. This is the common meat fly of India; it never enters houses. In India it is certainly not a specific myiasis-producing species. The larvas of argyrocephala are not well adapted to live in the tissues of man, for it has very poorly developed segmental spines in comparison with those of the larvas of *C. bezziana*, in which they are highly developed. *Lucilia argyricephala* is widely distributed in India, being found even at an altitude of 6000 ft. It is commonly infected with 3 varieties of flagellates, *Rhynchoidonomas luciliae*, which are found in its malpighian tubes, and *Herpetomonas muscea* and *domesticae* (Burnett) in its alimentary tract. The puparium is light brown in color, the posterior end is rounded. The processes on the eighth segment appear as dark brown spots. The eggs of *Lucilia cragii* (new species) are slightly larger than those of *Lucilia argyricephala*, measuring about  $\frac{1}{12}$  in. in length, and are light yellow in color. The number of eggs laid by a single female varies from 350 to 780. They are laid in a mass on the under side of the body of a bird or animal. The mature larvas measure about  $\frac{5}{8}$  in. in length and creamy white. *Lucilia cragii* is the common blow-fly of south India, occurring on the Pulneys, Sheoroys and Nilgris. It is very similar to the well-known European blow-flies, *Calliphora erythrocephala* and *C. vomitoria*. *Lucilia* breeds in nature in the dead bodies of birds and small animals, and its larvas are most efficient scavengers. It does not oviposit in living tissues. Both sexes are infected with *Herpetomonas mirabilis* and *H. muscae* and *domesticae*.

*Chrysomyia megacephala* Fabr. (Dux Esch.), the common Indian blue bottle, whose larvas occasionally cause cutaneous myiasis in animals, and *Chrysomyia nigriceps*, sp. nov., the common blue bottle of the Nilgris: Three cases caused by *Chrysomyia megacephala* Fabr. have been found in animals. The egg of this chrysomyia closely resembles that of *C. bezziana*. The mature larvas are  $\frac{9}{16}$  in. long and are whitish. The puparium is mahogany brown and has the same markings as the larvas. *C. megacephala* is primarily a necrophagous fly and breeds in a variety of food stuffs, but mainly on decomposing animal matter. Both sexes are commonly infected with flagellates. *Chrysomyia nigricephala* (Sp. Nov.) lays a lemon yellow egg  $\frac{1}{16}$  in. long. The female lays from 750 to 880 eggs in a mass. The mature larvas measure  $\frac{7}{12}$  in. The spines are not so well marked as in *C. megacephala*; they are wanting on the dorsal surface of the sixth and seventh segments. The anterior lip has pointed processes on each side of the midline. The spiral plates are large but not so large as those of the larvas of *megacephala*. The ninth segment is prominent and has a pointed fleshy process on each side. The puparium is mahogany brown and has the same markings and processes as the larvas.

*Chrysomyia albiceps* Wied. (Rufifacies Froggatt); one of the Australian sheep maggot flies, and *Chrysomyia villeneuvii*, sp. nov.: *Chrysomyia albiceps* (Wied.) is a widely distributed blow-fly. The egg is lemon yellow, is  $\frac{1}{16}$  in. long and slightly broader than that of the other species of Calliphorinae. The female lays from 300 to 450 eggs in a mass. The first stage larva is structurally like that of *C. megacephala* and *C. nigritis*. The mature larva is a little less than  $\frac{1}{2}$  in. long and grayish-yellow. The anterior end is markedly attenuated.

The first stage larva feeds on the decomposing body and after thirty-six hours changes to the second stage and begins to feed on larvae of other species. The third stage larvae feed entirely on other larvae. The puparium is dark brown in color, the dorsal surface markedly convex. It has the same processes as the larva. *C. albiceps* is a pest in Australia and has only within recent years taken to laying its eggs in soiled wool. There is no record of its feeding on other Calliphorinae in Australia. *Rufifacies* is identical with *albiceps*; this is of considerable importance to India for this fly may, in India, acquire habits similar to those it has acquired in Australia. The egg of *Chrysomyia villeneuvii*, sp. nov., is  $\frac{1}{2}$  in. long and is similar to that of the other species; the 2 chorionic ridges are more closely approximated. The mature larvae are  $\frac{1}{2}$  in. long, and dark gray throughout, the middle segments being darker. The first stage larva is exactly similar in structure to that of the other species. The third stage larvae are useful in India, as they destroy a large number of other blow-flies. The puparium is of a dark color and never becomes mahogany brown. It has all the signs and processes of the mature larvae. The species was first seen in Coonoor in March and at Kallar. Patton has not seen it in other localities.

*Lucilia pulchra* Wied. (*Rufucornis* Macq.), a larvivorous calliphorine, and *Lucilia ballardii*, sp. nov., a common south Indian blow-fly. *Lucilia pulchra* is the handsomest of Indian blow-flies. It occurs only in the plains. This species is viviparous and deposits its first stage larvae one at a time, either on human excrement or decomposing bodies of birds and animals. The mature larva measures  $\frac{1}{2}$  in. and is a dirty yellow color. The puparium is light brown and has the same markings as the mature larva. This species is essentially a flower and fruit juice feeder. The egg of *Lucilia ballardii*, sp. nov. is exactly similar to that of *L. Cragii*. The females are attracted to human excrement, but the eggs are never laid in excrement, but only in decomposing animal matter. The mature larva is  $\frac{1}{2}$  in. long and dirty white. The puparium, like that of other species, is dark brown and shows the same markings and processes as the mature larva. This species of *Lucilia*, unlike most others, has characteristic dark bands on the abdominal segments and also faint thoracic stripes. Very excellent colored illustrations show the characteristics of the thoracic and abdominal segments in these species of Calliphorinae.

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**The So-Called 'Penis' of the Bedbug (*Cimex Lectularius*) and the General Homologies of the Male and Female Genitals of This Insect.**

*S. R. Christophers and F. W. Cragg, Indian J. Med. Research, 9:445, Calcutta, Jan., 1922.*

The investigators have carried out a detailed study of this subject which is summarized as follows: (1) The abdominal segments in the bedbug have not so far been correctly notated. The condition in the nymph and other considerations, including a relic of the first tergite, the position of the last pair of spiracles and the relation of the segments to the genital passages, show that the large apparent first segment is the true second abdominal segment. (2) The female opening is be-

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hind the eighth sternite. The processes arising from the sternite are the gonapophyses of the eighth segment, or valvulae intermediae of some authors. The valvulae superiores (gonapods, styloids) though seen in some Heteroptera are absent in Cimex. The prominences on either side of the genital furrow are divided halves of the ninth sternite corresponding to the lateral chitinous portions of the sternal plate in the last instar nymph. (3) The male opening is behind the ninth sternite and between this and the tenth segment. The hollow in the ninth sternite (genital cavity) in which the male organs usually lie in the Heteroptera is reduced in Cimex to a tiny oval pouch enclosing the phallosome. The latter structure, so far overlooked, lies at the root of the so-called penis and has all the chief characters of the phallosome in the order generally, though greatly reduced in size and complexity. The grooved false penis is one of the pair of processes (lateral appendages of Sharp) present with few exceptions throughout Heteroptera and higher Homoptera. The groove does not function as a duct but is a sheath for the mososomal portion of the phallosome which can pass along it. (4) The sex can be distinguished exteriorly in the nymph, even when first hatched from the egg. (5) The so-called penis is formed by the development of one of the bilaterally arranged processes which arise from division of the primitive projections. The outgrowth on the left continues to develop, becoming the penis, while that on the right eventually disappears. The phallosome is formed from folds on either side of the early rudiment of the ejaculatory invagination and appears, as described by Zander for the Hymenoptera and Trichoptera, to be formed from the inner portions of the two primitive projections springing from the primitive genital cavity. The vas deferens and accessory glands develop from a pair of small globular rudiments, one on either side, which arise independently of the ejaculatory invagination of the epidermal layer and are terminal dilatations of tubes which pass down on either side of the testes. The ejaculatory duct is formed from an invagination of the epidermal layer which forms a spherical cavity with a button-like cellular plague on its anterior ventral wall. The spherical cavity becomes the ejaculatory duct of the adult. The lateral appendages of the Heteroptera, as far as can be judged from observations on Cimex, develop in the same manner as the valves of Zander.

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#### **1e. IMMUNOLOGY, SEROLOGY AND HEMATOLOGY**

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**The Twort-d'Hérelle Phenomenon. II. Lysis and Microbic Variation.**

*André Gratia, J. Exper. Med., 35:287, March 1, 1922.*

Since publication of the preceding paper reviewing the knowledge of the phenomenon of transmissible microbic lysis discovered by Twort and d'Herelle, there has been an opportunity to isolate a greater number of different types of *Bacillus coli*, all derived from the same original strain. The notion of contamination can be disregarded with certainty. When the few individuals still alive in a dissolved culture of *B. coli* are transplanted on slanted agar, a culture results which possesses (Sec. 1—Page 725)

new characteristics. First observed by Bordet and Ciua, this culture received the temporary name of modified coli. It was found in this study that this modified coli is very heterogeneous and that its 3 principal characteristics, resistance to lysis, lysogenic properties, and mucoid growth, are shared among different types of organisms that can be isolated when the normal original coli is plated together with increasing quantities of the lytic agent: (1) a certain number of bacilli are just resistant enough to survive and grow in the presence of a moderate quantity of lytic agent; (2) a few of the organisms are able to resist concentrated lytic agents and (3) among these only a few are mucoid. All these types are not motile and not fluorescent. A single strain of *B. coli* has been made to yield 11 different forms, all distinguished by striking characteristics, but still possessing the specific properties of *B. coli*. Nine of these forms have been submitted to antisera prepared with 3 different types. While 7 out of these 9 strains were agglutinated by any of the 3 antisera, only the original *B. coli* and the reversion to the original type were not agglutinable, even by their corresponding antiserum, which, however, agglutinated the other types.

It has been concluded that the different types observed are the result of changes occurring in the original *B. coli*. If the phenomenon is not due to a virus, the irregularity with which the phenomenon is promoted must find its cause in the bacteria themselves. In order to start the dissolution it is necessary to employ the proper forms of bacteria.

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**The Phenomenon of Bacteriophage.**

*Bernice Rhodes, J. Lab. & Clin. Med., 7:288, Feb., 1922.*

Rhodes suggests that a possible relation exists between immunity and bacteriophagy, a recently discovered phenomenon in the processes of autolysis in agar colonies, which, under certain conditions in bacterial cultures, possesses the property of destroying bacteria. A brief survey is given of the literature since the original article presented by F. W. Twort, in 1915, showing that the interest is apparently centered in the nature of the active principle, and its function in infection and immunity. A lytic substance is obtained from the feces or urine of a patient suffering from dysentery, and an emulsion is prepared in broth, the material being filtered.

Bordet and Ciua, by inoculating a guinea-pig intraperitoneally with several doses of *Bacillus coli*, obtained a peritoneal exudate which had this same property of dissolving or inhibiting a culture. The lytic principle referred to, demonstrable in young living cultures, is active against a number of different strains, and also against a number of related groups or organisms.

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**The Nature of the Bacteriophagic Virus.**

*Tai Watanabe, Wien. klin. Wechsnchr., 35:53, Jan. 19, 1922.*

Some authors, including Kabeshima, Bordet and Ciua, hold that a ferment-like substance in solution is the cause of the bacteriophagic action discovered by d'Herelle, while others, including d'Herelle and (Sec. 1—Page 726)

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Bail, think it is a minute, invisible body. But while d'Herelle thinks that it is a foreign element that destroys the bacteria, Bail thinks the bacteriophage is a special form or a derivative of the microorganisms themselves. When an emulsion of colon bacilli at 37° is allowed to dry on an agar plate and drops of bacteriophagic fluid are spread over it in a thin layer in places, the bacteria do not grow at all in the places touched by it if the fluid is strong, but if the bacteriophagic solution is weak there are isolated holes in the culture, showing that the bacteriophage action is brought about by formed elements, not by a substance in solution. The crenated edges, indicating the places at which there has been the greatest inhibition of growth by the drops of bacteriophage fluid, are formed by the confluence of a number of these holes. D'Herelle has used the plate method for counting the bacteriophage elements. This method also shows that certain bacteriophagi besides the specific ones have a nonspecific action on other species of bacteria. It remains to be determined whether this is due to a lack of specificity in action or to an admixture of another species of bacteria.

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**Transmissible Microbial Autolysis. D'Hérèlle's Bacteriophage.**

*Costa Cruz, Brazil-med. 36:45, Rio de Janeiro, Jan. 28, 1922.*

Study of proliferation of bacteria in the presence of bacteriophage and specific serum for the bacteria demonstrates that neither the serum anti-Shiga, nor the antibacteriophage Shiga, according to d'Herelle, acts directly to neutralize the bacteriophage. If we put together serum Shiga 3 c.c. and bacteriophage Shiga 16 gtt. in Martin's bouillon 10 c.c. and let the mixture stand for twenty-four hours, then add an adult culture of bacteria Shiga and let all stand for another twenty-four hours, filter, and add an emulsion of frozen bacteria, then repeat the whole procedure twice with an interval each time of twenty-four hours; it is found that free bacteriophage still persists in a perfectly active condition, after exhaustion of antibodies. The same is true when smaller quantities of serum are used. Hence, the inhibition of lysis can be explained only by an action of the serum upon the microorganisms. This confirms the fact that the bacteria which have fixed antibodies, when washed and treated by the bacteriophage, are not destroyed by the serum. It is easy to demonstrate that agglutination does not occur, because, for example, the Shiga serum, even in a titer strongly agglutinating for the *Bacillus Flexner* does not protect it against the action of the bacteriophage Flexner. Two amboceptors remainin; hence it seems premature to form a definite judgment on this point. There results a fact of great importance for the relations of the bacteriophage to immunity, namely, that the bacteriophage Shiga adheres to the microorganisms by the same process of affinity by which the latter fixes the antibody, which, in Ehrlich's language, amounts to a statement that the bacteriophage is identical with an antibody through its cytophile group.

If this is really so, it seems at the first glance that in the presence of a certain quantity of serum, no matter what is the quantity of bacteriophage added, there must always be the same proliferation of bacteria. But this is not what actually happens. In 3 out of 14 experiments there was no germination, in spite of the presence of serum.

Cruz believes the various antibodies for a particular microbe are bound to a like fraction of globulin, which, in the act of precipitation, carries with it the antibodies of which it is the subtracted albuminoid. However, it does not seem that without more examination we should abandon a hypothesis that the bacteriophage consists of 2 parts, one non-antigenic and the other antigenic, existing in our extracts and our microbes. What happens is that this inhibitory action of lysis upon antimicrobic specific serums greatly limits the rôle that we can attribute to the bacteriophage in the general processes of immunity. Assuming the likeness between specific serums for microbes and antibacteriophage serums, Cruz investigates the manner in which they proceed to the fixation of complement in the presence of heterologous bacteriophagi. If, as d'Hérelle affirms, the bacteriophage always takes part in the processes of vaccination, and if the bacteriophage has antigenic properties manifested by fixation of complement, it was to be hoped, since it is a unit, that specific serums, of whatever kind, must fix the complement in the presence of the bacteriophage Shiga. But this was not observed. Therefore it is seen that, if our serums are in fact antibacteriophage, the bacteriophagi fix the complement only in the presence of serums homologous to those bacteria on which they act.

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**The Relations between Antigen and Antibody Formation (the Influence of the Antigen Depot on the Formation of Antibodies).**

*E. Friedberger, Ztschr. f. Immunitätsf. u. exper. Ther., 33:306, Jena, Dec. 30, 1921.*

Sahli propounded the theory that all antibodies exist normally in a preformed condition in the blood. Treatment with an antigen links the antibody. Reduction of concentration results and that reduction stimulates the antibody-producing organs to renewed production, viz., to overproduction of antibodies. The following investigations show this theory to be erroneous: On Friedberger's initiative, Oshikawa examined the production of antibodies when an antigen depot is allowed to remain in the body for different periods. At the apex of the rabbit's ear (where there are fewest vessels) an antigen depot was established by intracutaneous or subcutaneous injection of *Proteus X<sub>19</sub>* bacilli killed at 60°. The depot was allowed to act for various periods following which it was removed by amputation of the whole ear and then the titer of the agglutination of the serum for the homologous series was continuously determined. It was shown that even when the ear was amputated only ten minutes after injection of a minimal culture quantity (1/100 loop in 0.1 c.c. sodium chlorid solution) the agglutination titer rose at least as high as when the ear was permitted to remain several hours, or even several days, and that this increased titer was maintained as long as in animals in whom amputation was delayed. Further, paradoxical behavior was observed, inasmuch as the agglutination in animals whose ears were not amputated was weaker than in animals in whom the ears were amputated at an early period. That the infinitesimal amounts of antigen, which are capable of being absorbed in such a brief space of time from the very small depot could form the substrate for the formation of antibodies when they reach the blood channel and the production sites of the antibodies, is diffi-

cult to believe, though not in itself impossible. But the fact that the production of antibodies should be less with longer absorption (when the ear is not amputated) would be inexplicable. Therefore the possibility of a second explanation must be admitted viz., that the antigen acts merely as a stimulant and that the secretion of antibodies so stimulated persists even after the elimination of the stimulation. On the other hand, if the depot is not removed, a part of the secreted antibodies is linked by the newly absorbed antigen. Hence the reduced titer in this case. The results of these researches render Sahli's theory untenable.

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**A Study on the Permeability of the Placenta. I. Permeability to Agglutinins, Hemolysins, Diphtheria Antitoxin and Diastase.**

*Helen Bourquin, Am. J. Physiol., 59:122, Feb. 1, 1922.*

The placental permeability of rabbits and guinea-pigs to diastase, agglutinins, hemolysins to sheep's corpuscles, and to diphtheria antitoxin was investigated. In the majority of the experiments the mother animal was killed by a blow over the head, the fetuses were immediately freed from the uterus, and the mother was bled from the heart by means of a syringe. The young were then anesthetized and the blood was drawn from the heart into a small syringe containing glass beads where it was defibrinated. In the majority of instances the rabbits were in the twenty-seventh to twenty-ninth day of the gestation period, the guinea-pigs between the fiftieth and sixtieth days. In all cases the placentas were examined for gross lesions, but nothing could be found which might be interpreted as such. One series of rabbits was immunized before conception with formalin-killed suspensions of pure strains of *B. coli*, of *B. paratyphosus A* and *B*, and of *B. typhosus* grown on a protein-free medium. In this way the results were not confused by a double immunization of the animal to the specific proteins of the bacillus and to the proteins of the culture media from which bacilli grown on culture media containing proteins cannot be entirely freed. All of these rabbits received a single injection of 1 c.c. of the antigen about eight days before term, to stimulate the maternal cells to more active production of antibodies. For the titration of the serum, a twenty-four hour culture of the same strain of bacillus grown on agar, formalin killed, and made to a concentration of 5 billion per cubic centimeter was used. Readings were recorded in terms of the actual amount of serum in the last tube showing distinct agglutination. Because of the small amounts of fetal serum available, 0.5 c.c. of the antigen, 0.5 c.c. or less of the serum dilution, and 0.85% salt solution to bring the quantity of the mixture to 1 c.c. were used. Maternal and fetal serums were run simultaneously, the antigen being added to the entire series at once just before putting them into the incubator. The tubes were incubated for one hour at 38° C. and read after standing for twenty-four hours in the refrigerator. Tubes containing the same amounts of serum were read throughout the entire series at the same time for the sake of more accurate comparison. A second series of rabbits and guinea-pigs was passively immunized by the injection of rabbit or guinea-pig immune serum respectively, containing a high titer of agglutinins. The technic was in all other respects as previously described.

For the test of permeability to hemolysins, rabbits were immunized before conception by injections of washed sheep's corpuscles and given a final injection of 2 c.c. corpuscles eight days before term. The technic was as described for agglutinins, except that in each tube, in titrating the serums, the dilutions of inactivated serum in amounts of 0.5 c.c. or less, 1½ units of fresh guinea-pig complement which had been diluted 1:20 with 0.85% salt solution, 0.5 c.c. 2.5% washed sheep's corpuscles, and salt solution to bring the amount to 1.5 c.c. were used.

To determine the permeability to antitoxin, one series of animals was used to test the transfer of diphtheria antitoxin from mother to fetus, a second to test the transfer from fetus to mother. In this series of experiments the fetus was injected in utero (the mother being under ether anesthesia) with an antitoxin containing approximately 1120 units of antitoxin per cubic centimeter.

For diastase a comparison was made of diastase in fetal and maternal serums under normal conditions, when the diastase content of the maternal blood was raised by ligation of the pancreatic duct and when the fetal blood diastase was raised by the injection of fresh rabbit diastase high serum obtained from animals with a ligated duct.

The tabulated results show that agglutinins and hemolysins tend to come to essentially the same concentration in the maternal and fetal blood, the difference between the two being relatively slight. Diphtheria antitoxin passes rapidly from fetus to mother, slowly from mother to fetus. The antitoxin used was a highly concentrated commercial product which the author believes may account for the difference between these results and those obtained with agglutinins and hemolysins. Normally the concentration of diastase in the fetal blood is lower than that of the maternal blood. An increase in the concentration of the maternal blood diastase is followed by a relatively slight increase in the diastase content of the fetal serum in some cases. The negative results and the low fetal values when the results are positive are probably accounted for by a great capacity on the part of the fetus to destroy or remove from the blood diastase in excess of the concentration normal to the blood.

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**The Formation of Antibodies by Transplanted Tissue.**

*K. Oshikawa, Ztschr. f. Immunitätsf. u. exper. Ther., 33:297, Jena, Dec. 30, 1921.*

By transplanting organs (hematopoietic system, kidney) from immunized animals to other animals of the same species, the formation of antibodies in the receiving animal was demonstrated. In an analogous manner experiments were conducted on the transplantation of portions of skin. Skin from a rabbit's ear was transplanted on the ear of another rabbit. It was shown that in this homeotransplantation, in contradistinction to autotransplantation, the transplanted tissue frequently failed to adhere even in animals of the same brood. But the success of transplantation is essential to the experiments. It transpired subsequently that following the transplantation of skin from actively immunized rabbits to normal rabbits, the formation of the respective antibody was detectable in the receiving animal (agglutination with bacillus paratyphosus, precipitation of egg-albumin, hemolysis). This formation of antibodies takes place in the receiving animal even

when injection of the antigen is performed a considerable time previous to transplantation. In that case the direct transference of antigen with the transplanted tissue is out of the question and the continued formation of antibodies on the part of the transplanted tissue must be assumed. The smoother the union of the transplanted tissue, the greater the formation of antibodies. When normal pieces of rabbit skin were placed in a goat's serum (hemolytic towards rabbit's blood) before transplantation, the serum had no influence on the process of union during the subsequent transplantation. Whether the goat's serum was inactive, or was rendered active by addition of complement, proved immaterial.

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**The Relation of the Hypophysis to Antibody Production.**

*Elliott C. Cutler, J. Exper. Med., 35:243, Feb., 1922.*

In guinea-pigs which had undergone a partial hypophysectomy immunization to *Bacillus typhosus* produced agglutinins in the same quantity and at the same rate as in controls which had not been operated on. The operation had no effect on typhoid agglutinins, hemagglutinins and hemolysins in animals already thus immunized. Feeding or injecting the gland did not affect the titer. The experiments would appear to indicate either that the hypophysis does not play an important direct or indirect part in the production of such bodies, or that a sufficient amount of hypophysis was left after the operation to exert the usual influence which the hypophysis may exercise in their production.

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**Sources of the Antibodies Developing after Repeated Transfusion.**

*Oswald H. Robertson and Peyton Rous, J. Exper. Med., 35:141, Feb., 1922.*

The authors desire to determine the source of the antibodies causing massive agglutination in the blood of animals which have repeatedly undergone transfusion. The agglutination has been traced to the antibodies elicited by the presence in the body of corpuscles originally found compatible. These are iso-agglutinins developing in the recipient and effective upon the alien elements circulating among its own cells. There are also genuine instances of induced auto-agglutination, in which the recipient's corpuscles, taken prior to transfusion and preserved in vitro, are agglutinated by the animal's own blood.

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**Studies on Heterophil Antigen and Antibody.**

*Tenji Taniguchi, J. Path. & Bacteriol., 25:77, Edinburgh, Jan., 1922.*

Friedberger, Hartock and Castelli demonstrated that the serum of rabbits, obtained after the injection of sheep's blood-corpuscles or serum, are powerfully toxic for guinea-pigs, and, on intravenous injection, cause death. Many other investigators have confirmed this fact. The clinical symptoms and postmortem appearances of animals treated in this way have been generally recognized as closely similar to those

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of guinea-pigs which have suffered from anaphylactic shock; this phenomenon has been termed by Friedberger antiserum anaphylaxis, in contrast to antigen-antibody anaphylaxis in the true sense. Working along these lines Tanguchi injected heterophile antigens and antibodies into guinea-pigs, and concluded after extensive experimentation that the anaphylactic symptoms caused by parenteral administration of heterophile antiserum into animals which contain heterophile antigen in their tissues, should be attributed mainly to the interaction between heterophile antigen and the antibody so introduced, altho the antiserum may also contain other molecules, which are toxic to the animal to a minor degree. The specific receptors for heterophile antibodies reside in the lipoid constituents of heterophile tissues. Aqueous suspensions of untreated heterophile tissues also exhibit specific reactions with heterophile antibody, but proteins from such tissues which have been deprived of their lipoid constituents lack the property. It is suggested that the molecules which react specifically to heterophile antibody in the animal are lipoids or lipoid-protein compounds, but not protein free from lipoids. Hence, the mechanism of heterophile anaphylaxis is to be regarded as distinct from that of anaphylaxis as originally described, where the specific receptors for the corresponding antibody are supposed to be proteins.

The development of anaphylactic shock by the reaction of specific lipoids and corresponding antibody would thus be established for the first time in the case of heterophile anaphylaxis. Normal serum of certain animals contains a varying amount of heterophile antibody; thus conditions for heterophile anaphylaxis are provided when such serum is injected into suitable animals. There is a question as to whether anaphylactic reactions may also develop as the result of injecting heterophile antigens into the human subject where a variable amount of heterophile antibody is naturally present.

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**The Solubility of Heterophil Receptors.**

Fritz Gutfeld, *Ztschr. f. Immunitätsf. u. exper. Ther.*, 33:472, Jena, Jan. 19, 1922.

The following experiment was carried out with: organ antiserum Ia of the titer 1:800 (on the day of the experiment); sheep's blood immune amoebocyte of the titer 1:1800; fresh horse kidney, chopped. The horse kidney (3 gm. in each case) was shaken for two hours at room temperature (1) with 30 c.c. N/100 NaOH, (2) with 30 c.c. N/100 HCl, (3) with 300 c.c. absolute alcohol. After settling, the liquids were filtered (partly by means of Berkefeld cylinders) until they were completely clear; then their quantity was determined (extracts). The residua were washed with physiologic NaCl solution; 1 gm. in each case was used for the experiment (residua). The extracts were inspissated on the water bath. What remained after evaporation was taken up with distilled water, neutralized, rendered isotonic (titrimetric control) and filled up to the original volume with physiologic NaCl solution. These isotonic neutral liquids were then filtered again until they were perfectly clear. Part of the extracts thus obtained were used for demonstrating, first of all, that the extracts in themselves have no hemolytic properties with respect to sheep's blood. Then followed the examination proper.

Series 1. (a) each of the 3 extracts (10 c.c.) was mixed with organ antiserum (60 solvent doses); (b) 1 gm. each of the residua (in 10 c.c. physiologic NaCl solution) was mixed with organ antiserum (60 solvent doses); (c) control; 60 solvent doses of organ antiserum were added to 10 c.c. of NaCl solution untreated. Series 2 was carried out in the same way, with the only difference that, in stead of organ antiserum, ordinary sheeps blood immune amboceptor (obtained by injection of sheeps blood) was added in the same quantity (60 solvent doses). Fixation for one hour in the water-bath at 37° C. was followed by filtration and qualitative valuation of the filtrates with respect to hemolytic properties. The results are tabulated. The extracts obtained by means of the 3 different menstruums as well as the residua remaining after extraction fix the total quantity of the heterogenetic amboceptor, whereas the hemolytic function of the isogenetic sheep's blood immune amboceptor (obtained by injection of sheep's blood) remains unaffected in all tubes alike. The 3 extracts which were employed contained, therefore, dissolved receptors which anchored the heterogenetic amboceptor in a specific manner. These results may be summarized as follows: Receptors from organs of the heterogenetic type may be brought to solution by various solvents. The dissolved receptor is demonstrable by the anchoring of the heterogenetic antibody. This anchoring is specific; it does not take place, if sheep's blood immune antiserum (obtained by injection of sheep's blood) is employed.

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**The Splitting Off of Bacteriolytic and Hemolytic Amboceptors.**

*H. Munter, Ztschr. f. Hyg. u. Infektionskrankh., 94:152, Berlin, Dec. 2, 1921.*

Experiments were performed to test the reversibility of bacteriolytic and hemolytic amboceptors. Bacterial colonies from an agar slant culture twenty-four hours old were washed off with 2.5 c.c. of physiologic saline solution, centrifugalized, and, after the remaining saline solution had been poured off, 5 c.c. of immune serum (in a dilution of 1:5) at a temperature of 8° C. was added to the bacterial sediment and left for twenty-four hours. Then the mixture was centrifugalized rapidly and, after the removal of the remaining saline solution, the centrifugalized bacteria were washed with 5 c.c. physiologic saline solution; the washing water was tested by animal experiments and in vitro, for the presence of immune bodies. Paratyphoid B., Shiga bacilli and vibrios were employed as bacteria. In the animal experiments Pfeiffer's method was employed. The quantity of the regained bacteriolytic antibodies were determined by tests with reagent-glasses, in accordance with the Neisser and Wechsberg method.

The hemolytic tests were performed as follows: Sheep-blood corpuscles free from serum were mixed with immune serum, centrifugalized and washed, and both the blood-corpuscle sediment and the washing water were tested as to their content of hemolytic amboceptors; to each 5% sheep-blood corpuscle infusion was added guinea-pig complement; this was kept for an hour at a temperature of 40° C., and then the results read.

The results of the experiments in accordance with those of other  
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authors, proved that protective antibodies (bacteriolysin) may be split off from bacteria, and that they may be demonstrated both by animal tests (Pfeiffer's method) and by tests with reagent glasses as well (bactericidal slides). It is also possible to detect split-off hemolytic amboceptors. The presence of fresh, unmixed blood corpuscles is not necessary for the test.

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**Experimental and Clinical Research of Antitrypsin.**

*St. Rusznyak, I. Barat and G. Daniel, Wien. Arch. f. inn. Med., 3:515, Jan. 20, 1922.*

The authors occupied themselves chiefly with 3 peculiarities of serum antitrypsin; the dialyzing power, the supposed lipoid nature, and the thermostability. (1) *Dialyzing Power*; the serum was examined with ultrafiltration according to Bechold, with a 7% colloid filter. Antitrypsin was never demonstrable in the filtrate, which means that the substance is not a crystalloid but is a colloid. (2) *Lipoid Nature*: dried serum was extracted with ether and chloroform. Antitrypsin was never found in the extract. This shows that it is not lipoid in nature. (3) *Thermostability*: (a) marked dilution of the serum contained antitrypsin in spite of heating. (b) Different sera react in different ways. Certain temperatures will damage some while not inactivating others. This means that there are several kinds of antitrypsin.

*Clinical Use in the Diagnosis of Carcinoma.* The method is unsuitable because the antityptic index merely shows the cachexia and the latter may be caused by various conditions. The positive results in cachectic carcinoma were 82.8%, and in cachexia due to other causes there were 48% of positive results. It is possible to say that a positive result speaks rather for than against carcinoma. It is perhaps possible to so develop the use of the test so that consideration may be taken of individual differences in the thermoresistance.

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**Studies on Agglutination with the Aid of the Centrifuge.  
The Influence of Temperature on Absorption and Flocculation.**

*Frederick L. Gates, J. Exper. Med., 35:63, Jan., 1922.*

The flocculation of bacteria which have absorbed specific agglutinins may be mechanically effected by means of the centrifuge, with results which coincide with those obtained by the standard method of test. Mixtures of immune serum and meningococcus suspensions were centrifuged for ten minutes at 1800 revolutions per minute, after having been incubated together; after centrifugalization the tubes were shaken and read by transmitted light, evidences of agglutination being unmistakable. It was found that the velocity of the absorption reaction is a function of the temperature at which it occurs, and that the presence of an excess of antibodies greatly accelerates absorption and flocculation.

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The Process of Agglutination on the Basis of the Agglutination Optimum. Influence of Sodium Chlorid Dilution on the Antibodies of Serums.

*Georg Heuer, Ztschr. f. Hyg. u. Infektionskrankh., 95:100, Berlin, Jan. 17, 1922.*

Heuer subjected the well-known fact, that from a certain concentration optimum the agglutination sometimes decreases in stronger concentrations, to an experimental investigation, using highly agglutinable typhoid, paratyphoid, Flexner, and "Y" strains. The concentration which corresponds to the agglutination optimum is higher, the lower the quantity of NaCl solution contained in the dilution liquid. If physiologic NaCl solution is employed for the dilution of the specific serum, the optimum corresponds to a serum dilution of 1:100 to 1:200; if normal serum is used instead of NaCl, the optimum corresponds to a concentration of 1:10 to 1:20; if normal serum mixed with NaCl solution in the proportion of 1:10 is employed for the dilution, the optimum is 1:20, 1:40, or 1:80; if the normal serum is mixed with NaCl solution in the proportion of 1:1000, the optimum is 1:80, 1:100, or 1:200. This progression of the optimum in accordance with the quantity of NaCl solution contained in the dilution liquid is regularly observed with respect to all bacteria and all kinds of serum. From this it may be inferred that the phenomenon is not of a biologically specific nature, but dependent on physicochemical conditions.

But the decisive factor in regard to the progression of the optimum is neither the NaCl content nor the hydrogen-ion concentration; nor are the surface tension figures, as determined by Traube's stalagmometer, of any significance in regard to the agglutination optimum. The real factor to which the phenomenon of the agglutination optimum and its variability according to the character of the dilution liquid must be referred is the property of the normal serum which enables it to arrest agglutination by the retention of the agglutinins. In order to find out the quantities of the retained agglutinins, experiments were undertaken for the purpose of determining the titer of the specific serum without any addition of NaCl solution. To that end, it was necessary first of all to remove the normal agglutinins contained in the normal serums employed for the dilution. This was effected by saturating the normal serum with the bacteria in question, the agglutination of which was to be examined. Normal serums employed for the dilution after removing the normal agglutinins regularly caused a considerable decrease of the agglutination titer, as compared with the series diluted with NaCl solution, with respect to all the specific serums and all the bacteria that were subjected to examination. The titer rises in proportion to increased addition of NaCl solution (but not of sodium chloride in substance); when, in the course of that increase, 100 c.c. physiologic NaCl solution are added to 1 c.c. normal serum, the titer becomes equal to that corresponding to a pure dilution with NaCl solution. In the series diluted with pure normal serum, the titer was found to be 1:400, as compared with 1:10,000 in the NaCl series; accordingly, 96% of the agglutinin units established in the NaCl series are masked by normal serum. The experiments exclude the possibility of holding the agglutinoids responsible for this behavior; otherwise, the absurdity would result that they would be ineffective in a dilution of

1:10 of the normal serum series, but effective in a dilution of 1:80-100. Without straining the facts, therefore, one can only look upon the retention of the agglutinins in the normal serum as the cause. This retention is believed to be due to the presence of a protective colloid; it would seem that serum albumin should be considered above all others in that respect; it, as a more stable and more highly dispersed elements, holds the more labile globulins in solution, including the agglutinins. The more the albumins are diluted or rather separated from one another by the addition of NaCl solution, the smaller the quantity of agglutinins which are retained by them; the point at which the retention of agglutinins ceases defines the agglutination optimum. In other words, the agglutinins are liberated by the NaCl solution. This appears to be true also in regard to other albuminous antibodies.

The normal agglutinins may also be removed from the serum by heterologous bacteria and would therefore seem to be colloidchemically different from the specific agglutinins. In contradistinction to the normal agglutinins, the specific agglutinins derived from the specific serums for a special kind of bacteria, as well as the metagglutinins, can bind the homologous bacteria only if the serum is diluted with NaCl solution in the proportion of 1:100.

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**Researches on Racial Biology by Means of Isohemagglutinins.**

*F. Versar and O. Weszczsky, Biochim. Ztschr., 126:33, Berlin, Dec. 27, 1921.*

According to the experiments of Landsteiner the blood-corpuscles of some individuals are agglutinated by the blood serum of others. Four groups of individuals may be differentiated. The red blood-corpuscles of the first group are agglutinated by the serums of the 3 others, those of the second group by the serum of the third, those of the third group by the serum of the second and lastly those of the fourth are not agglutinated by any of the serums. In other words, the blood-corpuscles of group 2 have the property A, those of group 3 have the property B. There are other individuals who have property A and B (group 1) and those who have neither of the two (group 4). The percentage figures of the different groups examined in Hungary are the following: group 1, 16.9%; group 2, 37.3%; group 3, 18.3%; group 4, 27.5%. The Viennese figures are: group 1, 4.6%, group 2, 47.6%; group 3, 12.2%; group 4, 35.3%. The question was raised of whether these facts were not the expressions of racial differences. Therefore, new experiments were carried out to ascertain whether different races which lived side by side under similar conditions for centuries would show any differences regarding their isohemagglutinins. The 3 races examined were Hungarians from Debreczin, Germans from the vicinity of Budapest and Gypsies from Bihar and Heves.

The experiment was carried out in the following manner: To 2 drops 5-10% saline suspension of the red blood-corpuscles which were to be examined, 1-2 drops of the test serum of group A and of group B were added, and the mixture put into a test-tube. If the blood-corpuscles agglutinated only with serum A, then the individual belonged to group B (3), if on the other hand the agglutination took place with

both serums, then group A B (1) was present, but if they did not agglutinate with either of the serums, then neither group A nor B (4) was present. The results of the agglutination were read after half an hour ( $37^{\circ}$  C.) and again after eighteen hours ( $20^{\circ}$  C.); they were tabulated and compared with the experiments of Dungern and Hirschfeld.

The experiments show that these 3 races which have mixed for three centuries, can still be singled out by their isoagglutinins: the Hungarians still show, after more than twelve centuries of separation from other peoples of very ancient Turko-Mongolian race the same arrangement of groups as these. The same is true of the Germans, who have been separated from their kindred for more than two centuries, and is also true of the Gypsies, whose period of separation amounts to at least six hundred years. In the last race, a complete accordance with the Indians was proven. The relative frequency of the 2 isoagglutinins A and B is, therefore, a racial character by which races can be differentiated, even after centuries.

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**The Significance of the Group Hemagglutination in Free Transplantation and the Changes in the Agglutination Groups Produced by Medicaments, Narcosis and Exposure to X-Ray.**

Rudolf Eden, *Deutsch. med. Wochenschr.*, 48:85, Berlin, Jan. 19, 1922.

It is possible to determine to which group the blood donor or receiver belongs with a few minutes' use of the microscope and use of a standard serum according to Brem's modification of the method of Moss.

There are 4 groups. The serum of group I does not agglutinate at all while the serum of group IV agglutinates the red blood cells of groups I-III. The red blood cells of group I are agglutinated by serums II-IV, those of the last (IV) group are not agglutinated by any serum. The serum and red blood cells of II and III stand in mutual relation to the other groups. The schema shows that the donor and receiver should belong to the same group. Combinations of some of the groups is not dangerous while it may be dangerous with others. The test sera are from group II and III and it is possible to read from the scale, after microscopical examination, to which group the donor or receiver belongs. Actual clumping and not mere rouleaux formation is of significance.

American surgeons also use the test before transplantation. Eden has noticed a poor result in 4 cases of epidermis transplantation in which the people were of the same agglutination group. Physico-chemical processes which influence colloids are apparently changed in regard to the same titer as read off from the transplantation table. It is the inflammation at the site of the transplantation which causes the changes. Eden performed experiments with various medicaments and exposures to x-ray. He found that agglutination of erythrocytes with certain agglutinins does not remain constant in the same subject, so that a person does not belong to the same group under all circumstances. Changes may be caused by medicaments and processes which have the property of changing colloids. The patients remain in the same group during the normal course of life. There is an occasional change

during menstruation. The group of the donor and receiver should be determined before transfusion because the condition may be changed by medicaments and narcosis. Medicaments given after transfusion may have an unlooked-for effect on the red cells which were given to the patient.

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**The Adsorption of Bacteria and Agglutinins by-Suspensions and Colloids.**

*Leo Bleyer, Ztschr. f. Immunitätsf. u. exper. Ther., 33:478, Jena, Jan. 19, 1922.*

Experiment: 4 c.c. of a 2% suspension of animal charcoal, bolus alba, calcium oxalate and barium sulphate was shaken five or ten minutes with 1 c.c. of an emulsion of bacteria (paratyphoid A, staphylococci, Friedländer's Bacillus pneumoniae); 0.5 c.c. of the filtrate was then planted and the colonies counted. Result: animal charcoal and calcium oxalate showed 100% adsorption, bolus alba a smaller percentage, and barium sulphate least of all. Bacillus pneumoniae was adsorbed most readily (perhaps on account of the capsules), and paratyphoid A with the greatest difficulty. A control of the experiment by centrifugation showed that, by the latter alone, the original quantity of bacteria is diminished by five-sixths, so that the effect of the powder must be considered as slight. In neither of the 2 experiments could a parallelism be established between the size of the granules and the degree of adsorption. The decisive factor, therefore, would seem to be the magnitude of the surface development of the adsorbent. In that respect, the animal charcoal, which is of very slight weight and of fine suspension and porosity ("inner surface"), is particularly effective as an adsorbent. The heavy barium sulphate is least effective. With the exception of the animal charcoal, the percentage of the adsorption decreases, as the chain of bacteria increases.

In order to examine the adsorbability of immune serums, the following experiments were carried out: (1) A 10% suspension of animal charcoal, calcium oxalate, bolus alba, kaolin, BaSO<sub>4</sub>, and diatomaceous earth was mixed in equal parts with different serums, allowed to stand for an hour at 37° C., then centrifuged, filtered and titrated with respect to the agglutinins. The animal charcoal was far superior to any of the other substances in regard to the constancy and intensity of its effect. Next in order, but at a considerable distance, was bolus alba; the adsorption of infusorial earth and barium sulphate was incomplete and uncertain. (2) To 0.5 serum dilution were added: concentrated calcium aluminate, BaCl<sub>2</sub>, concentrated Fe<sub>2</sub>C1<sub>6</sub>, concentrated gypsum water, O. S. N. AgNO<sub>3</sub>. For the purpose of precipitation were then further added: 10% Na<sub>2</sub>CO<sub>3</sub>, 5% Na<sub>2</sub>SO<sub>4</sub>, 10% Na<sub>2</sub>CO<sub>3</sub>, ammonium oxalate, and 20% NaCl. Then followed centrifugation and titration. The result was that only the slowly sintering deposit of BaSO<sub>4</sub> was able to bind the agglutinin, whereas the rapidly precipitated silver chlorid and the gelatinous deposit of aluminum hydroxid gave positive results only in rare cases. (3) The following colloids were examined: Colloidal ferric hydroxid electroferrol, electrocollargol, caseosan were digested one hour with serum dilution at 37° C., after which the colloid was precipitated by the addition of 0.4 c.c. 10% NaCl or 0.4 c.c. 30% HCl respectively. After centrifugation, the decantations were neu-

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tralized by 30% NaOH and titrated. Result: The metal hydrosols precipitated the agglutinin independently of temperature, duration of action and electric character. The effect of caseosan was inconstant. These experiments led to the further question of whether the process of the adsorption of the immune body is reversible. For this purpose, the deposit was again colloidized after precipitation by the addition of 2 c.c. of 4% NaOH and subsequent shaking, and then titrated. It was found that in contact with a homologous suspension of bacteria, the agglutinin can be detached from the metal particles, thus leading to agglutination. On the other hand, it is not possible to disrupt the agglutinin colloid combination merely by heat and the addition of NaOH (without addition of bacteria).

In regard to the question as to whether the adsorption of the agglutinins was parallel to the precipitation of protein from the immune serum, the following result was established: the 2 processes correspond to each other, if the immune serum is acted upon by animal charcoal or metal hydrosols; but in suspensions such as kaolin or barium sulphate, the deproteinization is much more intensive than the absorption of the agglutinins.

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#### The Action of Various Metallic Salts on Hemolysis.

*Helen A. Purdy and L. E. Walbum, J. Immunol., 7:35, Jan., 1922.*

This investigation was undertaken to find out the significance of the presence of small quantities of metallic salts on the hemolytic action of saponin on horses' blood corpuscles, of staphylococcal lysis on goats' blood corpuscles and of complement amboceptor on sheep's blood corpuscles. The minimal concentration of the respective metallic salts at which their action is measurable is determined as follows: To a series of test-tubes containing decreasing doses of the metallic salts is added hemolysin in such a quantity as to produce only a slight hemolysis; after filling up with a physiological salt solution to the volume stated, the blood corpuscle suspension is added, this mixture being then, after shaking, placed in the thermostat and afterwards in the ice-box over night. The next day a determination is made of how much hemoglobin has been dissolved in each tube. The technic used with the saponin and staphylococcal lysis is centrifugalization of the defibrinated blood which is washed twice in 0.9% salt solution, and from these washed corpuscles, the preparation of a suspension. To this is added the metallic salts and saponin, staphylococcal lysis or complement amboceptor. It was found that by determining the minimal dose of the individual salts at which their action is demonstrable, it is possible to obtain a comparison of the actions of different salts. Some of the salts exert an inciting action on hemolysis and others exert an inhibitory one. At one concentration the salts are ineffectual; at another inhibitory.

Experiments with the maximal concentrations of the various metallic salts that can be applied without producing hemolysis, agglutination or discoloration of the blood corpuscles indicate that the stability of such blood corpuscles towards the action of hemolytic substances is found to vary greatly. Experiments were made to determine whether the action of these salts was due to the cation or to the anion. Chlorides, sulphates and nitrates of Mg, Mn, Zn, and Ni were used. It was found in all cases that the anion was without significance in this respect.

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**Dissimilar Nutrition as the Cause of Changing Sensitiveness and Altered Antigenic Qualities of Bacteria.**

*C. E. Cahn-Bronner, Ztschr. f. Immunitätsf. u. exper. Ther., 33:375, Jena, Dec. 30, 1921.*

A comparison of cultures of the same paratyphoid-B strain grown in bouillon and in a lactic acid-ammonia culture medium gave the following results: (1) The retarded development of germs by chemical disinfectants affects principally the assimilatory side of bacterial metabolism because quinin, salicylic acid, trypaflavin, phenol and mercuric chlorid retard more powerfully in a lactic-acid-ammonia culture medium than in bouillon. This difference is not altered by bettering the simple culture medium with grape-sugar and it is only equalized by the addition of an amino-acid, or of peptone. (2) The germs grown in a simple artificial culture medium are more sensitive to germicidal chemical influences. Bacteria grown in lactic acid-ammonia culture mediums are destroyed by phenol and mercuric chlorid in a shorter time after they are transferred to sodium chlorid solution than the bouillon culture of the same strain when transferred to such a solution. Smaller amounts of mercuric chlorid suffice for the destruction of the lactic-acid-ammonia cultures. (3) The multiplication of paratyphoid-B bacilli and Gärtner bacilli in lactic-acid-ammonia culture mediums is retarded by temperatures that permit their rapid growth in bouillon. The germs that develop with difficulty in a simple artificial culture medium are destroyed by a lower temperature, after their transfer to sodium chlorid solution, than bouillon bacteria transferred to such a solution. (4) Paratyphoid-B bacilli and Gärtner bacilli grown in lactic acid-ammonia culture mediums are agglutinated more strongly and in more numerous pH by the Michaelis and Beniasch acid agglutination than when grown in bouillon cultures. (5) Paratyphoid-B bacilli grown in lactic-acid-ammonia culture medium are agglutinated less strongly by paratyphoid-B immune serums, whether these are produced with lactic-acid-ammonia cultures or with bouillon cultures, and they are influenced less by heterologous serums, or typhoid and Gärtner serums, than bouillon bacteria of the same strain. (6) Extracts from lactic-acid-ammonia cultures give stronger precipitations with paratyphoid-B immune serum, whether the extracts are obtained from lactic acid-ammonia bacteria or bouillon bacteria, than extracts from bouillon bacteria of the same paratyphoid-B strain. (7) From these facts it may be concluded that germs whose growth took place under great synthetic functions in lactic-acid-ammonia culture mediums have a different material composition from those grown in bouillon. This difference, however, does not extend beyond the limits that divide one race of bacteria from another. The serological differences between bouillon bacteria and lactic-acid-ammonia bacteria are not of the same kind as those between well-nourished and starving bouillon bacteria. During the growth in a simple artificial culture medium, merely a quantitative displacement of single body constituents toward each other takes place while in prolonged undernutrition complete deficiency of ectoplasmatic body constituents is brought about in addition.

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**The Rôle of the Dilute Acids in Infection.**

*I. Walker Hall and A. D. Fraser, Bristol Med.-Chir. J., 38:158, Dec., 1921.*

In experiments not yet concluded, Hall and Fraser have developed an important application in the technic of blood cultures. It was found that when bacteria are subjected to minute alterations of acidity obtained by the use of different types of acids, their growth may be accelerated or retarded. For instance, 1/200 n/nitric acid or 1/200 n/lactic acid stimulates the growth of streptococci, while 1/100 n/citric acid retards it. So, throughout the whole range of pyogenic and other organisms, there are to be found H ions with the other ions, or anions—in this case, nitrates and lactates—which catalyze the ordinary growth of organisms. With diphtheria bacilli, phosphoric, lactic and nitric derived ions act as stimulants, while the saturated monobasic fatty acids, such as formic, butyric and propionic, retard development. When it is remembered that the pH of the duodenal contents controls the prepyloric sphincter and the rate of outflow from the stomach, and that sputum contains areas varying in their pH content, and that local pH alterations are necessary for the effective performance of physiological functions, as well as for adequate response to infections, it is evident that a careful survey of the associated factors is called for. There are questions of the influence of the minute pH ranges in the tissues as they affect the acceleration or retardation during bacterial invasion; the possibility of inhibiting the growth of organisms in purulent conditions of local areas, so that diphtheria bacilli cannot attain their necessary alkaline surroundings for the production of toxin; and a damaging pH of tissues, so that the diagnosis of experimental inoculation may be hastened. Hall and Fraser have not been able to turn a harmless germ into a pathogen (Much) but have raised the virulence of pneumococci by methods similar to those of Much—injecting lactic acid together with saprophytic bacteria into the animal. By altering the pH of the blood media, an earlier and higher percentage of positive results were obtained and a means was previsioned for concomitant estimation of the exact bacteriolytic resistance manifested by the patient.

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**Studies of Superinfection.**

*Bruno Lange, Ztschr. f. Hyg. u. Infektionskrank., 94:135, Berlin, Dec. 2, 1921.*

The so-called resistance against infection, i. e., the resistance of chronically diseased animals against superinfection, was studied, especially in regard to tuberculosis and syphilis—*infections of a pronounced chronic character*. It is possible to establish immunity against superinfection not only in cases of chronic infectious disease such as tuberculosis, syphilis, Texas fever, trypanosome diseases and malaria, but also in the acute infections, such as chicken-cholera and paratyphoid. The condition is that a certain, although incomplete, immunity against the infective agent develops in the species of animals in question.

The object of these experimental studies was to furnish data concerning superinfection. Experiments were first performed with chicken-cholera infection in guinea-pigs for the reason that when the same  
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exceedingly virulent culture was used, the animals acquired a chronic infection or an acute daily fresh infection, according to whether the injection was made subcutaneously or intraperitoneally. The experiments were performed in such a manner that the primary injections were made subcutaneously into the abdomen or into the lumbar region. The secondary, with 10 times the daily dose, was made from twenty-four to forty-eight hours later. Similar experiments were also performed with mouse-typoid and Gärtner's bacilli, also on mice, and then with streptococci and pneumococci on rabbits.

The experiments demonstrated that a few days following the primary injection a certain immunity against superinfection appeared in the injected animals. In cases of chicken-cholera in guinea-pigs, this immunity was seemingly lacking in the beginning or was very slight. The secondary injections were therefore varied in time of administration. A pronounced immunity was observed in guinea-pigs when they were examined three weeks after the primary injection. Only a comparatively slight immunity was produced in the experiments with mouse-typoid and infection with Gärtner's bacilli, due to the fact that mice immunity was produced in rabbits against streptococcal and pneumococcal infection. These animals are easily immunized against the infections in question. This may perhaps be attributed to the fact that such good results may be obtained only under especially favorable conditions, especially only with cultures with an average virulence. In cases of all infections against which it is possible to immunize, the immunity appears very soon after the primary infection with killed antigen. Ehrlich and Hata observed this fact in connection with their experiments with spirochetosis in chickens, in which the immunity was very pronounced twenty-four hours after the primary treatment, and was complete in forty-nine hours. In cases of infection of guinea-pigs with chicken-cholera and of mice with mouse-typoid, the organism in question is apparently unable to produce enough antibodies, i. e., to create an immunity sufficient to render the exciting bacterium totally harmless. In such cases, the conditions are also present under which a chronic latent or recurrent infection may appear, which in turn may be considered as an expression of an incomplete, labile and at the most an uncertain immunity.

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Depression Immunity in Intravenous Superinfection with Streptococci.

J. Morgenroth and L. Abraham, *Ztschr. f. Hyg. u. Infektionskrankh.*, 94:163, Berlin, Dec. 2, 1921.

The immunity against superinfection due to direct inoculation into the circulation of the virus producing secondary infection, in cases of tuberculosis, has been established by various authors. This form of immunity (depression immunity) was studied in respect to its presence in superinfection with streptococci. The primary infection occurred subcutaneously, intraperitoneally and intravenously. Immunity was observed in mice in twenty-four hours, and also after two or three days. This immunity following subcutaneous, intraperitoneal and intravenous

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chronic primary infection with streptococci, and directed against the acute intravenous secondary infection with streptococci, causes a more or less pronounced delay in the fatal issue, or may even prevent death.

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**On *B. Welchii* Hemotoxin and Its Neutralization with Antitoxin.**

*Herbert Henry, J. Path. & Bacteriol., 25:1, Edinburgh, Jan., 1922.*

The report deals with an in vitro investigation of the hemolyzing substance present in *Bacillus welchii*, the method employed being a modification of that originally devised by Madsen for the study of tetanolysin. Throughout the series the hemotoxic unitage has been standardized when necessary by titration against freshly prepared 1% solution of the same specimen of a precipitated toxin. *B. welchii* produces in cultures a hemotoxin the potency of which can be measured in vitro; the same substance is found in the precipitate obtained from filtrates by treatment with ammonium sulphate or alcohol. The hemolytic titre was tested on washed red cells of rabbits. The effect of various temperatures was tested on culture filtrates and toxins precipitated by alcohol. The lytic value of *B. welchii* toxins stored in the cold and examined at weekly intervals over a period of six weeks showed no marked depreciation in lytic capacity. When incubated at 38°C., and examined at two day intervals over a period of ten days there was no detectable depreciation in lytic value after two days incubation, but exposure to this temperature for longer periods resulted in a loss of lytic capacity, which at the end of ten days' incubation amounted to about half the original total. Toxins were heated to 60°C., 80°C., and 100°C. The bulk of the hemotoxin which is rendered inactive at 60°C. disappears after five minutes' heating; the remaining unadulterated hemotoxin loses its lytic value slowly on longer heating at 60°C. Similar results were obtained at 80°C and 100°C. Even after boiling for fifteen minutes hemotoxin is still present in measurable quantities.

A series of neutralization experiments showed that hemotoxin could be neutralized by *B. welchii* antitoxin. A table shows how rapidly the combination takes place at 38°C. The slight lag that occurs in the case of precipitated specimens of hemotoxin is attributable to the mass of hemotoxin which these preparations contain. The complete neutralization experiments showed that the neutralization of this hemotoxin follows the law of multiple proportions. In the fractional saturation experiments, the hemotoxin content of the toxin under test was estimated; then the amount of antitoxin which gave complete neutralization of 1.0 c.c. of the toxin was determined and finally equal amounts of toxin, usually 1.0 c.c., were put up with gradually increasing fractions of the 1.0 c.c. neutralizing doses of antitoxins. For one hour these were left in contact at 38°C. and were then titrated out, so as to determine the amount of unneutralized hemotoxin contained in each. With the fresh culture filtrates the first few fractions of antitoxin neutralize the bulk of the hemotoxin. If the toxin has been stored for several months, the first fraction of antitoxin neutralizes little or no hemotoxin. With precipitated toxins the initial lag in neutralization becomes still more marked. Graphs of the results are not unlike those obtained by Madsen for tetanolysin.

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**The Transmission of Agglutinins of Bacillus Abortus from Cow to Calf in the Colostrum.**

*Ralph B. Little and Marion L. Orcutt, J. Exper. Med., 35:161, Feb., 1922.*

In the work on infectious abortion associated with *Bacillus abortus*, the authors have found, from a study of the agglutinins in the blood-serum of mother and fetus, that agglutinins against this organism are obtained by the calf from the mother through the colostrum. Calves at birth are without agglutinins.

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**The Purification and Concentration by Desiccation of Hog Cholera Immune Serum.**

*Charles W. Duval and Maurice Couret, J. M. Res., 42:503, Oct.-Dec., 1921.*

Although the loss of live-stock from hog cholera has considerably decreased as a result of the general use of serum therapy, the need of a prophylactic agent of greater potency and duration is felt, and Duval and Couret undertook this study to determine a more powerful and staple anti-hog cholera serum than the one in use.

Immune serum, it was found, can be rapidly desiccated in vacuo at 0° C. without damage to its antitoxic property, and the residue can be pulverized and kept in sealed glass containers, probably for years, without alteration. A refined and concentrated product has obviously greater protective value than has the same amount of crude defibrinated blood. Since it has been determined that the immune substance of the blood is contained in the plasma only, the cellular elements, which amount to 6%, are worthless and should be eliminated before the serum is desiccated. From 100 mg. of desiccated material 1 c.c. of the cell-free serum is obtained while the same quantity of defibrinated hog's blood yields 156 mg.

To concentrate the serum, the desiccated powder is dissolved in a small volume of sterile distilled water or normal saline, 1 gm. antitoxin powder, the equivalent of 10 c.c. pure serum or 15 c.c. defibrinated blood, readily dissolving in 2 c.c. water, concentrating the volume of antitoxin 10 times. The advantage of this method is that instead of 30 c.c. crude hemolysed defibrinated blood, the dose commonly used in practice, the entire amount of protective substances is given in 3 c.c. of fluid. The antitoxin may be kept in the powdered state until ready for use. Desiccation makes possible the utilization of low-grade sera which otherwise would have little value; and the employment of a smaller volume of fluid and, consequently, of a greater number of antitoxin units.

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**The Action of Diphtheria Toxin upon the Circulation.**

*S. Yabe, J. Pharmacol. & Exper. Ther., 19:1, Feb., 1922.*

The effects of diphtheria toxin on the circulation and respiration appear several hours after its injection, even when a dose that is many times that ultimately fatal is injected intravenously. All attempts to analyze its action in acute experiments are therefore futile. Further

light can be thrown on its effects only by examining the condition of animals subjected to it several hours previously, and comparing their symptoms with those of controls. In a series of such experiments, the blood pressure was found to be lower than in the controls, and this appeared to be due to the failure of the central vasomotor mechanism. No evidence of direct action on the peripheral vasoconstrictor nerves, or on the vessels of the heart, was obtained.

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**Bacillus Diphtheriae. Immunologic Types; Toxin-Antitoxin Relationship.**

*W. H. Parson and Edward Redowitz, J. Immunol., 7:69, Jan., 1922.*

Very recently Havens described 2 distinct groups of *B. diphtheriae* existing among the virulent strains, as differentiated by the agglutination reaction. He found that the neutralization of group 1 toxin was complete, of group 2, partial or incomplete. Paxton and Redowitz undertook their investigation in an attempt to corroborate Havens' results. They obtained from various laboratories 7 strains of *B. diphtheriae*. The cultures were grouped by the agglutination reaction and then toxins were prepared from 2 strains of each group and tested against group 1 antitoxin. Diphtheria antitoxin is universally prepared only from strains that fall in the first and largest group. In tables of the protection tests, one can see that the neutralizing power of standard antitoxin is equally effective against group 1 and group 2. All the results of these experiments were contrary to the contention, that group 2 toxin is not neutralized by standard antitoxin to the same extent as group 1 toxin. One, one and a half and two units of standard antitoxin injected simultaneously with large doses of virulent cultures, protect guinea-pigs against both types of *B. diphtheriae*. By the results of the experiments, it is concluded that diphtheria antitoxin as produced by the injection of toxin obtained from group 1 strains, neutralized equally well the toxins produced by either group 1 or group 2 organisms.

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**Experimental Studies of the Nasopharyngeal Secretions from Influenza Patients. VI. Immunity Reactions.**

*Peter K. Olitsky and Frederick L. Gates, J. Exper. Med., 35:1, Jan., 1922.*

Rabbits were injected with the anaerobic, filter-passing microorganism, *Bacterium pneumosintes*. After various periods the authors reinjected material from nasopharyngeal washings, from lungs of affected rabbits, and from *Bacterium pneumosintes*. Typical experimental protocols for the various cases are given. The active material appears to be of antigenic nature, so that rabbits are protected from the effects of a second inoculation. They conclude that the experiments also indicate the antigenic identity of the various strains of the agent from different sources. The protection in the experiment of longest duration was found to last for at least fourteen months. The experiments described furnish additional evidence of the pathogenic character and the virtual identity of the strains of active agent derived from the nasopharyngeal secretions of influenzal patients.

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**Effects of Pneumococcus Type I on Leukocytes and Hemopoietic Organs.**

*M. S. Tongs, J. Infect. Dis., 30:323, March, 1922.*

In order to study the leukocytic reaction in pneumococcus infections, Tongs carried out experiments on rabbits and guinea-pigs. He found that the leukocytic reaction in rabbits infected with Pneumococcus type I is somewhat dependent on the virulence of the organisms, a low virulence producing leukocytosis and a high virulence leukopenia. The leukopenia seems to be brought about by degeneration of leukocytes and of cells in the hemopoietic organs, this degeneration apparently being due to the toxic action of the pneumococcus. After an intraperitoneal inoculation of guinea-pigs with virulent and nonvirulent pneumococci, the leukocytes as a rule show phagocytosis. In certain instances the failure of the leukocytes to take up highly virulent pneumococci seems to be due to intoxication of the cells as evidenced by degenerative changes. It appears that virulent pneumococci also produce a chemotactic substance, since although the leukocytes may fail to ingest virulent cocci they usually become surrounded by them.

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**An Allergic Reaction of the Tuberculous Uterine Horn.**

*G. H. Smith, J. Immunol., 7:47, Jan., 1922.*

The experiments in this investigation are an application of the principle of specific reactivity between antigen and its homologous antibody, employing the uterus of the tuberculous guinea-pig as an indicator. The tests were performed by suspending a uterine horn from a tuberculous guinea-pig and a horn from a normal guinea-pig in the same bath of oxygenated Locke's solution. After relaxation of the horns and the appearance of the regular rhythmic contractions, urine from a known tuberculous case was added to the bath (350 c.c.), usually in 3 to 5 c.c. amounts. This amount of urine from any of the tuberculous cases never induced a marked reaction in the normal horn while in some cases the tuberculous horn responded sharply. This reaction of the tuberculous horn was not simply an increased susceptibility to urine in itself; as indicated in repeated experiments by first using normal urine, to which no response was secured, and then after washing and renewing the bath, adding a tuberculous urine which induced an immediate contraction of the horn from the infected animal. From known cases 8 tuberculous urines were used and with 7 of these, reactions of the tuberculous horn were secured of greater or less intensity as compared with the normal tissue.

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**Antigenic Properties of Tuberculin.**

*E. Seligmann and F. Klopstock, Ztschr. f. Immunitätsf. u. exper. Ther., 33:467, Jena, Jan. 19, 1922.*

Clinically, the tuberculin reaction represents the purest type of a specific hypersensitivity reaction; biologically, it differs in important points from the thoroughly investigated forms of anaphylaxis. Clinical and therapeutic experiences are in favor of a specific effect of tuber-

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culin, although the latter manifests itself only under special conditions, i.e., in the tuberculous organism. But the biologic demonstration of the antigenic nature of tuberculin has not by any means been cleared up so far. Wassermann and Bruck based their interpretation of the tuberculin reaction and of the specific circumscribed phenomena on the antigenic character of tuberculin, whereas more recently, Selter has, on the contrary, based his irritant substance theory on the very absence of antigenic properties. In an effort to excite hypersensitivity reactions in healthy guinea-pigs by means of old tuberculin, the technic and results were as follows : (1) One preliminary subcutaneous application of 0.1-0.2 c.c. old tuberculin was followed by intravenous reinjection of 0.1 c.c. old tuberculin after three weeks without result. (2) Repeated preliminary subcutaneous application and intravenous reinjection led to decrease of temperature in 2 out of 4 animals. (3) Repeated preliminary intracutaneous application followed by intravenous reinjection in 6 experiments produced decrease of temperature in 1 case. (4) Preliminary application, alternately subcutaneous and intracutaneous; and intravenous reinjection in 12 experiments brought the result that 6 animals died of anaphylactic shock and the other 6 exhibited more or less pronounced symptoms of shock, from which they recovered. Control was made by preliminary application of glycerin bouillon and intravenous reinjection of old tuberculin. None of the animals showed appreciable anaphylactic symptoms. The sensitization of healthy guinea-pigs was further demonstrated by the following observations: (1) flaring-up of the old places of injection after subcutaneous incorporation of an additional quantity of tuberculin within twenty-four hours, (2) arthus phenomenon, extensive edematous infiltrations at the place of inoculation after repeated subcutaneous injections. From these experiments it appears that the specific sensitization of guinea-pigs by means of intensive and repeated preliminary application of old tuberculin is feasible.

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**Specific Reactions to the Contents of Vesicles.**

*E. Thomas and W. Arnold, Münch. med. Wchnschr., 69:196, Feb. 10, 1922.*

If cantharides collodion is applied over a positive Pirquet intracutaneous reaction, producing a vesicle, and if the contents of this vesicle are mixed in a proportion of 1 to 5 with physiologic salt solution, and tuberculous children are vaccinated with this mixture, the majority of cases react more strongly than they do to twice the amount of tuberculin alone. This would seem to indicate that substances are present in the contents of a vesicle over a tuberculin reaction, which strengthen the reaction. Experiments with the contents of vesicles produced over non-specific inflammations, gave negative results. In cases where the Pirquet reaction was so intense as to produce a vesicle, the contents of the vesicle contents were inactivated by heating to 60°, the reaction was weakened.

An examination of the cell contents of cantharides vesicles showed only slight signs of an inflammatory exudate, so that these contents are adapted for a study of most questions of a biological nature. It is a tissue fluid which is very little changed and which cannot be obtained

in any other way. Its characteristics in the different infectious diseases and its content in gummy substances should be carefully examined. It is easy to fill these vesicles with any desired fluid. A needle is stuck under the epidermis about 0.5 cm. away from the vesicle, pushed into the vesicle from below and to one side and the vesicle is emptied. It can now be filled through the same needle. The vesicle can thus be used as a living chamber and the changes brought about in the fluid introduced can be studied later. Therapeutic experiments can also be made in this way.

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**Differentiation of the So-Called Acid-Fast Bacteria by Means of Complement Fixation.**

*H. Schlossberger and W. Pfannenstiel, Ztschr. f. Hyg. u. Infektskrh., 95:77, Berlin, Jan. 17, 1922.*

By ordinary methods, it is sometimes impossible to distinguish acid-fast saprophytes from the genuine tubercle bacilli, which are pathogenic with respect to warm-blooded animals. On the one hand, races of genuine tubercle bacilli may lose their pathogenic character in consequence of continued cultivation in an artificial culture medium to such a degree that even large doses cause only local transformation in guinea-pigs at the point of inoculation. On the other hand, saprophytic acid-fast bacteria, by passing again and again through warm-blooded animals, may gradually approach the genuine tubercle bacilli very closely in regard to pathogenicity, staining, and cultural behavior. The authors therefore tried to arrive at a differential diagnosis by serologic methods. Agglutination cannot be employed, since it could hardly be possible to produce perfectly homogeneous suspensions of the acid-fast bacteria, which usually have a tendency to spontaneous agglutination. Author therefore endeavored to accomplish the differentiation of the various races by complement-fixation experiments with prepared immune serums. But this proved to be impossible, because the complement fixation shows pronounced group specificity. Only one single race of chicken-tuberculosis bacilli constantly showed preponderant reaction with the homologous serum in a stronger dilution than with the heterologous serums. The different behavior of this one race was probably caused, not only by a different composition of the antigen apparatus, but also by physicochemical differences.

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**The Complement-Fixation Reaction by Means of Besredka's Antigen as a Serologic Indicator of Tuberculosis.**

*W. Janusz, Polska gaz. lek. 1:7, Warsaw, Jan. 1, 1922.*

To obtain an active antigen, Besredka uses a nutrient egg medium. He prepares an emulsion of 20 yolks and 1 liter of sterilized neutral water, and clarifies it by the gradual addition of a 1% solution of sodium hydroxid. After clarification, 7 liters of water are added, the solution is poured into Roux's bottles and heated at 110° for twenty minutes. This is an excellent nutrient medium for tubercle bacteria. After four days the culture is sterilized by heating, and is made homogeneous by shaking. It is particularly suitable as an antigen for the fixation of complement.

The investigations of many writers seem to indicate that Besredka's antigen produces specific results in the reaction of complement-fixation. Positive results indicate the existence of tuberculosis, and negative results indicate its absence. In 90% of all patients with phthises, the reaction is positive, while in nonphthisic patients it is almost always negative. In 104 cases of tuberculosis of the skin the results were negative only in 17 cases, while they were positive 69 times and doubtful 18 times.

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**Specific Partial Functions of the Typhoid-Immune Body and Their Effect on the Biology of Paratyphoid Bacilli.**

*Tr. Baumgärtel, Ztschr. f. Hyg. u. Infektionskrankh. 94:386, Berlin, Dec. 2, 1921.*

The studies are based upon statistical notes concerning the cultural findings in specimens consisting of 25,000 blood-gall cultures. Experiments revealed a reduction and temporary retardation of the reaction of typhoid bacilli in blood immunized against typhoid fever; on the basis of a similar retardation of the reaction of paratyphoid A bacilli the presumption of an analogous reduction of the propagation of paratyphoid bacilli seems justified. As a matter of fact, a retarding effect on the reaction of paratyphoid bacilli in blood immunized against typhoid was observed during the experiments. Another instance was observed. The cultural and serobiologic characteristics of the paratyphoid strains grown during the retardation of the reaction deviated from the normal in such a manner that they could be identified only after several reinjections. These atypic forms represent morphologic, biologic and serologic variations of cultural characteristics of the bacilli. The atypic cultural characteristics of the typhoid strains cultured from blood immunized against typhoid were due to the effect of antibodies occurring in the organism, or possibly to a reaction of bacterial cells analogous to bacterial immunity, due to structural adaptation. Numerous distinctive retardations of growth and phenomena of variability were observed in the paratyphoid strains at a time when the examination of blood in regard to antibody reactions had given a negative result. The decrease and increase of typhoid agglutinins was also markedly dependent upon the interval of time between disease and the protective injection. The explanation of the origin and correlations of this evidently functional symptom complex is necessary for the solution of this problem. It was therefore necessary to consider especially such atypic forms as were outside the range of variation, furthermore only such cultural anomalies were considered to be typical as had no intimate connection with the external conditions of the cultural procedure. The seroreaction was regarded from the standpoint of ensuring both the character of the bacterial antigen and the individual production of antibodies. In studying the serologic condition, it was necessary to consider not only the normal serologic connections between typhoid and paratyphoid, but also the relations between typhoid and paratyphoid in the blood immunized against typhoid. Through a careful study of the literature the anomalies were grouped in accordance with the variation types and variation factors. It was possible to distinguish 3 various groups of the atypic paratyphoid cultures. Most of the cultural peculiarities came within the normal limits of range of the biologic

variation. A small number could be defined as constantly atypic. The third group represents the temporarily atypic paratyphoid cultures in which, in the sense of reversible group variations, a complete, functionally coherent complex of manifestations of life forms variations. These temporarily atypic variations were considered as degenerative phenomena of age and corresponded with the cultural and serobiologic anomalies of paratyphoid cultures isolated from blood immunized against typhoid. These analogous cultural anomalies were due to a deformative, regressive influence.

As variation factors one may assume the reduction of the bacterial growth energy, caused by the technic of the reaction, physiognoc-nutritional or serologic retardation factors. In estimating the time of blood-letting, the stage of the disease, and the temperature of the body were considered, and in regard to the quantity of blood necessary for the tests, the absolute quantity of blood and the concentration of the blood-gall were considered. Blood, ox bile and Endo's nutritive bodies were taken into consideration in studying the physiognoc-nutritional variation factors. A critical examination revealed that all these factors could be eliminated as causes of the disturbance of growth observed, and it was therefore presumed that the atypical cultural forms were caused by a serobiologic variation factor. This must be understood as a partial function of the immune bodies produced through immunization against typhoid. The sero-anomalies depended upon the peculiar behavior of the typhoid agglutinin during the paratyphoid infection.

For better disclosure of the condition, the seroreactions in paratyphoid cases and the reactions in healthy persons immunized against typhoid were arranged statistically. The experiments indicate that a retardation of paratyphoid A bacilli was observed in 35.3% of the cases and retardation of paratyphoid B bacilli in 52.8% of the cases. The typhoid and the paratyphoid agglutinin content apparently had a reciprocal relation and were simultaneously an expression of an immunization change of the infected organism. In cases of paratyphoid A and of paratyphoid B a reduction of the typhoid agglutinin content was observed in the beginning of the disease and during the course. It was also observed that a distinctive species relationship exists between the typhoid and the paratyphoid agglutinins. The serologic relationship of *B. paratyphosus A* to *B. typhosus* is less than that of *B. paratyphosus B*. Paratyphoid agglutinins often exist in blood immunized against typhoid; the agglutinin most frequently found is paratyphoid B agglutinin (partial agglutinins). These partial agglutinins are unspecific and are therefore diagnostically useless. It was further observed that the retardation of the paratyphoid bacillary reaction occurred in a great number of cases in which the result of a simultaneous Gruber's serum reaction did not indicate the nature of the specific paratyphoid antibody action. A characteristic of these cases with retarded bacillary reaction was the functional connection which was always present between the bacilli and the immunization against typhoid. The biologic species relationship between the typhoid and paratyphoid bacilli was determined on the basis of immunization relationships between typhoid and paratyphoid agglutinins in the blood immunized against typhoid. It was also observed that *B. paratyphosus A*, which is epidemiologically, clinically and culturally closely related to *B. typhosus*, differs from the *B. paratyphosus B*, which culturally is less closely related to typhoid

The retardation phenomena were therefore most frequent in cases of paratyphoid B.

In patients with paratyphoid who had been immunized against typhoid, a primary reduction of the typhoid agglutination was generally observed in the beginning of the disease, and a secondary increase of the typhoid agglutinin during the process of the paratyphoid infection. These changes of typhoid agglutination were usually followed by a similar change of paratyphoid agglutinin.

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**The Receptor Apparatus in the Paratyphoid Group.**

*F. Schiff, Ztschr. f. Immunitätsf. u. exper. Ther., 33:511, Jena, Jan. 19, 1922.*

The final result established by these investigations is as follows. *Bacillus paratyphosus B* may be distinguished from *Bacillus breslaviensis* by the fact that, in addition to common thermostable and thermolabile receptors, the bacilli have specific thermolabile receptors. In order to clear up the mutual relations, it was necessary to employ a considerable series of serums, for analysis was rendered difficult by the fact that not every immune or patient's serum contains antibodies against all types of receptors.

By means of valuation and fixation experiments, a series of genuine races of *paratyphosus B* and one of *breslaviensis* were examined. For this purpose, Schiff employed monovalent immune serums, which he had prepared against some genuine races of the 2 species, and also serums of patients who exhibited the clinical aspect of *typhus abdominalis*, and from whose blood *Bacillus paratyphosus B* had been cultivated. It was found that serologic differences could regularly be demonstrated between the genuine *B. parathyphosus B* and the *typhus breslaviensis* (meat-poisoning) of the paratyphoid group: (1) The differences were demonstrable, if immune serums are employed, by means of the receptor analysis according to the Weil-Felix method. In this way, the following information was gained concerning the receptor apparatus of the 2 groups of bacteria: (a) both groups possess thermostable and thermolabile receptors; (b) the thermostable receptors of both groups are identical; the thermolabile ones are in part different, some are common to both groups, but there are others which are specific to one or the other of the 2 groups. (2) The monovalent immune serums contain, in accordance with the receptors, "gross" and "fine" flocculating agglutinins in the sense of Weil and Felix, which, in this connection, are also called "labilotropic" and "stabilotropic," according to their relations to the thermolabile and thermostable receptors. By observing the type of agglutination and by precipitation experiments, it is possible to demonstrate (a) stabilotropic agglutinins, directed against the thermostable receptors common to the *B. paratyphosus B* and the *B. breslaviensis*; (b) labilotropic agglutinins, which are nonspecific in the same sense; (c) labilotropic agglutinins specific for *B. paratyphosus B*; (d) labilotropic agglutinins specific for *B. breslaviensis*.

(3) Paratyphoid B patients' serums may contain "gross" as well as "fine" flocculating agglutinins. The former are directed either against one part of the thermolabile receptors (in some cases against

the part which is common to both groups, and in others against the specific part) or against both parts at the same time.

(4) The agglutinins of the examined normal serums of man, horse, ox, pig, sheep, rabbit, guinea-pig are of the "fine" flocculating type and can be precipitated by heated bacteria, i.e., they are stabilitropic. It has not been possible so far to demonstrate the presence of "gross" flocculating agglutinins in the normal serum, which are directed against the labile bacterial receptors. This behavior is analogous to that of the sheep's blood hemolysins in normal serums, as examined by Forssman and Friedemann, which are also stabilitropic.

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**Experiments Concerning the Presence of Virulicide Substances in the Blood of Vaccinated and Revaccinated Persons.**

*S. Fujii, Ztschr. f. Immunitätsf. u. exper. Ther., 33:443, Jena, Jan. 19, 1922.*

As only a few isolated observations have been recorded so far concerning the virulicide power of the human blood after vaccination, Fujii investigated this problem by experiments carried out on 15 persons by the following method: First of all, a specimen of the serum was obtained and tested as to its virulicide power, 0.2 c.c. serum or serum dilution (1:50) remaining in the incubator with 0.2 c.c. diluted (1:50) lymph for two hours. Five drops of this mixture were applied to rabbits' corneas which had been scarified in a lattice-shaped pattern, the reaction being examined every day. Control experiments on 4 unvaccinated persons showed the absence of any virulicide power. The experiments with the serum of vaccinated and revaccinated persons (one to four years having passed since vaccination) showed that the undiluted serum exerted an appreciable virulicide power (attenuation of the reaction) only in the case of 2 persons, whereas, in a serum dilution of 1:2, the virulicity was no longer demonstrable. Finally, 6 persons were revaccinated. But no essential change of the virulicide power of the serum was observed within 3-4 weeks. It is noteworthy that the virulicity, even though it was present in a few cases to a slight degree, did not permit of any conclusion concerning the result of the vaccination. From these experiments, Fujii infers that, in the case of man, the immunizing effect of vaccination does not correspond to the formation or the regeneration of virulicide antibodies.

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**The Protective Action of the Cerebrospinal Fluid in the Mastic Reaction.**

*Karl Presser and Alfred Weintraub, Ztschr. f. Immunitätsf. u. exper. Ther., 33:317, Jena, Dec. 30, 1921.*

It is known that the normal cerebrospinal fluid possesses a protective action which prevents the flocculation of a mastic solution by sodium chlorid solution. In certain diseases, however, (paralysis) the fluid loses its protective action so that mastic solution (1% alcoholic solution in 4 times the amount of distilled water) is flocculated by sodium chlorid solution in spite of the addition of the fluid. The protective action is usually ascribed to colloids (albumin bodies). On

the other hand it is shown that when the fluid is digested with pure animal-charcoal albumin and lipoids are completely eliminated (absorption), it, nevertheless, retains its protective action. Also, when the fluid is dialyzed the nonalbuminous external dialysate has a protective action. Consequently, no part in the protective action is ascribable to the colloidal albumins. The protective action, then, depends only on the alkalinity of the fluid. The alkalinity of the normal and of the pathological fluid amounts to 0.2 c.c. tenth-normal caustic soda (by the gas chain method, in normal fluid pH—8.7, in pathological fluid pH—8.6). By the addition of a corresponding amount of tenth-normal lye, a solution of sodium chlorid acquires the same protective action as that of the fluid and, further, the fluid loses its protective power on being neutralized. By the dialysis of the fluid against a large volume of flowing water an internal dialysate is obtained, which has lost its alkalinity, but retained its colloids. The colloids, though precipitated from solution, may be redissolved by addition of sodium chlorid. This internal dialysate does not prevent the flocculation of mastic solution by a solution of sodium chlorid. The positive flocculation reaction in syphilitic fluid seems to depend on the fact that the protective action of the alkali is eliminated by increased, and probably also by chemically-altered, albumin. Ammonium chlorid-ammonia-buffer solutions protect mastic solution against flocculation by sodium chlorid with an equal or even a lower pH than that possessed by the fluid.

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**The Chemical Composition of the Floccules Formed during the Serologic Syphilis Reaction.**

*Emil Epstein and Fritz Paul, Deutsch. med. Wchnschr., 48:89, Berlin, Jan. 19, 1922.*

The results of Klostermann and Weisbach, as published in the Deutsche Medizinische Wochenschrift, No. 37, 1921, show that the flakes produced in the Sachs-Georgi reaction consist not only of lipoids of the extract but also of a considerable quantity of albumins from the serum. This is contrary to the views of Epstein, Paul and others, who found that the flakes consist only of lipoids. The albumin in the remains of the flakes which are insoluble in ether weighs 4 mg. as found by Klostermann and Weisbach. This is probably due to an error in the test caused by washing the flakes which appeared in the salt solution, in distilled water. This precipitate has no relation to the precipitate seen in the reaction itself. The N value of the remains of the flake precipitate is due exclusively to the N contained in the lipid extract. The experiments show that it is absolutely impossible that there is any relation between the demonstrable N value of the flake precipitate and the flaked out albumin. There is certainty no important quantitative connection. The results of Klostermann and Weisbach cannot interfere with the value and certainty of the demonstration that the flakes formed in positive sera in the Meinicke reaction (D.M.R.), as well as in the Sachs-Georgi and Wassermann reactions, are exclusively formed from the lipoids. Klostermann and Weisbach were unable to demonstrate the actual presence of appreciable quantities of albumin in the precipitate of the Sachs-Georgi reaction.

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The Significance of the Proportion of Sodium Chlorid in Regard to the Reactivity of Active Serums in the Serologic Diagnosis of Syphilis by Flocculation.

F. Georgi and H. Lebenstein, *Ztschr. f. Immunitätsf. u. exper. Ther.*, 33:503, Jena, Jan. 19, 1922.

In the Sachs-Georgi reaction, as well as in Meinicke III, the discrepancy, as compared with the results of the Wassermann reaction, may be removed, if a 1.5 or 2% solution of NaCl is used as medium instead of 0.85%. If inactive serums are employed, the concentration of the NaCl solution seems to be irrelevant with respect to Meinicke III. In some cases, the stabilization required for the Meinicke III reaction is affected by merely letting the active serum stand for some time. The authors explain these facts by assuming that active serum contains inhibitors, which may be neutralized (1) by a higher proportion of NaCl, or (2) inactivation, or (3) by mere keeping. From these observations, it appears that the Meinicke III reaction is essentially identical with the Sachs-Georgi reaction.

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Studies on Complement Fixation. V. The Hemolytic versus Fixability Powers of Complement.

R. L. Kahn and Ethel D. White, *J. Infect. Dis.*, 30:313, March 1922.

It has been widely accepted among complement-fixation workers that no relation exists between the hemolytic and fixability powers of complement; that a given complement may be capable of laking corpuscles in the presence of specific hemolysin and not be capable of being "fixed" by some specific antigen-antibody complexes. This study was made with a view of finding nonfixable complements and determining the underlying cause or causes for their nonfixability. The hemolytic tests were carried out with a sheep-cell-guinea-pig-complement system and the fixability tests, with an alcoholic extract antigen of beef-heart and syphilitic serums. In these studies no complement which contained moderate amounts of natural amboceptor was used. In the fixability tests, the complement was used in carefully titrated 2-unit quantities and fixation was carried out for four hours at icebox temperature.

Of 478 guinea-pig complements, representing 275 separate pigs, tested for fixability, not one was found which lacked this property. On the other hand, it was found that with an average dilution of 1:10 of highly potent complement (instead of 2 units), a one-hour fixation period in the water-bath (instead of four hours in the icebox), and a positive serum which just approaches 4+, the fixation ranged from 2+ to negative in practically every case. The authors' results indicate, therefore, that so far as syphilitic serums and Wassermann antigens are concerned, the so-called nonfixability of some complements reported by certain investigators may be apparent rather than real, and that if all precautions are taken to overcome those factors in complement fixation which may lead to false negative results, complements which possess hemolytic properties will be found to be fixable also.

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**The Conservation of Complement.**

*J. Hammerschmidt, Münch. med. Wchnschr., 69:122, Jan. 27, 1922.*

Hammerschmidt suggested (Münch. med. Wchnschr. No. 48/1920) the conservation of the complement serum in a Wassermann reaction by adding a 10% solution of sodium acetate, as this would render the Wassermann reaction cheaper. Klein (Münch. med. Wchnschr. No. 45/1921) rejects this method, because he found in the course of his investigations that the conserved complement of the preliminary test, though it retained its lytic properties, frequently produced a negative reaction when the controlling serums indicated a positive result; he also noticed a nonspecific inhibition in 7-day old serum. The first phenomenon he explains by bacterial contamination of the conserved complement, and the latter by a disappearance of complement. Hammerschmidt has used the method of conservation for over a year and has never discovered any of the disadvantages mentioned by Klein. It is true that he collects and conserves the complement surrounded by all possible conditions of sterility, so that bacterial contaminations can hardly occur. The conserved complement is used within a week, and during this period even Klein could not discover any disappearance of complement.

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**Examination of the Cholesterin Content and Its Significance in Relation to the Antigens Used in the Wassermann Reaction.**

*Miklos, Frank, Orvosi hetil., 66:45, Budapest, Jan. 29, 1922.*

The substitution of known substances for the antigen in the Wassermann reaction has not been satisfactory. The importance of the lipoids was emphasized by the recent use of cholesterin antigens in the Wassermann and Sachs-Georgi reactions. Miklos determined the cholesterin content of the various antigens and the nature of the significance of cholesterin in the Wassermann reaction. The cholesterin content of the different antigens was determined by the method of Bloor which depends on the reaction of Liebermann-Burchard. One c.c. of the antigen was heated on the electric oven and extracted 4-5 times with chemically pure chloroform. The volume of the extract containing the cholesterin was made up to 5 c.c. with chloroform and 2 c.c. of anhydrous acetic acid and 0.1 c.c. of concentrated sulphuric acid were added. The mixture remained in the dark for fifteen minutes and the determination was made with a colorimeter according to Autenrieth. The quantity of cholesterin varied from 0.014-0.033% in 6 antigens. The percentage of cholesterin content of the antigens showed varying values and no conclusions could be drawn. The result is different if the quantity of active antigen, that is, the cholesterin content of the antigen, is absolutely determined according to a certain titer. The result shows that the value of the cholesterin actually functioning in a given experiment varies within narrow limits, 13-16 (1-0.001 mg.). The author comes to the following conclusion: (1) it is possible to determine the absolute quantity of cholesterin in a Wassermann reaction if the cholesterin content of the antigen and the titer are known. (2) The result of the Wassermann reaction does not change if the Wassermann reaction is performed with the same antigens even if the dilutions

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vary. The same result was obtained and no change was noted when the same antigens were used in different concentrations without correction of the volume by addition of physiological salt solution.

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### **Specific Precipitin Test for Human Semen.**

*Ludwig Hektoen, J. A. M. A., 78:704, March 11, 1922.*

Many years ago it was found that rabbits injected intraperitoneally with semen developed specific antisemen precipitins. A table given shows that, in rabbits, injections of mixed human semen, obtained from many different men, produced precipitins for human serum and for human semen, and that the precipitins for human serum may be removed by elective absorption, the rabbit serum now containing precipitins specific for human semen only. On the other hand, treatment of the antiserum with semen dilutions removes all precipitins. Numerous tests of spots of various kinds, containing seminal and other protein substances, have been made with antiserum, from which precipitins for serum proteins had been removed, that is, with "treated" serum, in order to study its power to deduct human seminal proteins under different conditions. The results indicate that antiserum for human semen may be of practical value in detecting by its specific precipitin reaction the presence of human seminal protein in suspected spots and stains.

It is of special interest to note that the precipitin reaction for semen seems to be not only specific for the species, but also semispecific, that is, limited to constituents of the semen of that species. The more exact nature and source of the specific elements in human semen invite investigation, but it may be stated now that extracts of carefully washed spermatozoa give precipitates with antisemen serum.

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### **Hydrogen Ion Studies. II. Changes in the Reaction of Serum on Thermal Destruction of Complement.**

*Edwin F. Hirsch and Ebba C. Peters, J. Infect. Dis., 30:263, March, 1922.*

The destruction by heat (56° C.) of complement in normal guinea-pig and rabbit serum is accompanied by changes in the pH. These probably are caused by dissociation of the complement substance or substances, the dissociation occurring with the liberation of an acid radical, which spontaneously and with heating is volatilized or is removed by combining with some other substance. The pH of the serum appears to be the factor determining how much of this acid radical is present as such.

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### **Relationship of Various Antigen Serums.**

*Moyer S. Fleisher, J. Immunol. 7:51, Jan., 1922.*

In Fleisher's studies concerning tissue specificity, he was continually faced with the fact that the various tissues showed great complexity of relationship. He performed about 50 experiments, using various organs (liver, kidney, brain), to analyze the influence of 3 potential factors in bringing about the absorbent-antigen relationship, and

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by these experiments he demonstrated that absorption of an antiorgan serum by a combination of tissues removes more antibodies than does absorption by a single one of these tissues. This phenomenon depends upon a qualitative rather than a quantitative variation of absorbing activity of the tissues, which in some degree is specific for each tissue. This specificity or individuality of each tissue may depend upon any of the 3 potential factors which are: (1) the better absorbent quality of any particular tissue; (2) the existence of a relationship between certain organs permitting the nonhomologous tissue to react constantly more strongly with another particular tissue; and (3) the existence in each organ of not only the particular homologous specific substances but also of substances specific with other organs.

The basis of the experiments was the absorption of the various antiorgan sera with the various tissues and the subsequent testing of the complement-fixing power of the sera with various antigens. Fleisher concludes that there exist apparently, in the various tissues, substances or chemical compounds which are definitely related to and show a specificity for certain substances contained in other tissues. However, it is not certain that these nonhomologous tissue specific substances are chemically and immunologically identical with the tissue-specific substance of the particular tissues. They may be only similar. The demonstration of this type of antigen in the tissue and of the corresponding antibody in the antiserum adds only to the evidence of the complexity of these tissue antigens and antibodies. Since Fleisher used the entire organ, he expected that he would find the interpretation of his results complicated by this fact, but it was possible to dissociate and analyze the various immunological relations of the component parts of these complex antigens.

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**Nonspecific Reactions with Precipitating Antiseraums.**

*P. Manteufel and H. Beger, Ztschr. f. Immunitätsf. u. exper. Ther., 33:348, Jena, Dec. 30, 1921.*

As a result of recent publications, particularly of Friedberger and Collier's investigations, the specificity of precipitin reactions was questioned not only as to theory but serious doubts were cast on the practical applicability of the reactions. The forensically important differentiation of human blood and, further, the identification of albumins (meat) of different species by the precipitin reaction with test serums, which is of importance in the control of food stuffs, appeared to be uncertain. Therefore, Manteufel and Beger tested a large number of antiseraums in the bacteriological section of the Imperial Health Bureau for the nonspecific precipitin reaction. They themselves prepared a part of these serums, and a part was ready for practical use. (The relationship reaction, for instance that existing among ruminants, is to be considered a specific reaction). The homologous serum was employed, instead of organic albumin, as antigen for these tests. Of 67 different serum specimens 42, or 63%, were fully specific and gave no trace of reaction with heterologous antigens even in dilution of 1:200 to 1:100. In 16, or 24%, nonspecific reaction was found with this strong concentration but not in the concentration used in actual practice of 1:1000, so that these serums, too, may be used in practice (total, therefore, equals 58, or 87% suitable for practical purposes). With

heterologous antigen at 1:1000, 9 antiserums gave a weak reaction, but even with these a wrong diagnosis was hardly possible as the specific reaction is always much stronger and takes place always in much higher dilutions than the nonspecific reaction. Manteufel and Beger were unable to observe, with the material at their command, that nonspecific reactions take place in a definite kind of serum or are absent in another kind. On the other hand, Friedberger and Collier found, in 5 out of 7 horse antiserums they tested, a nonspecific reaction with mutton albumin of the same strength as the specific reaction. Manteufel and Beger were able to produce heterogenetic amboceptors with certainty only by immunization with organic albumin and not with serum albumin. The method described by Friedberger and Collier, in which antiserums that showed encroachment of the reaction to nonspecific species of albumin are rendered purely specific by saturation with the nonspecific antigen, gave the authors a negative result (in the trials of the serums which produced slight heterogenous clouding in high concentrations). The encroachment of the reaction of Greifswalder antiserums described by Friedberger and his coworkers cannot be referred to heterogenetic antibodies but to another as yet unknown cause. The reliability of albumin differentiation with reliable precipitating serums is not questioned. Serums showing heterologous clouding in the absolutely essential subsequent examination can not be employed for practical purposes. As the precipitation of these serums signifies a great economic loss, everything is to be avoided in the preparation that may promote the formation of bodies having nonspecific reactions. Above all, only fresh substances are to be employed as antigens, or at least such as have not as yet suffered any decomposition of the specific properties pertaining to the species. Serums kept long in the fluid state lose antigenic properties, though they remain sterile, and the antiserums produced from such serums show a greater tendency to heterologous clouding. To prevent heterologous precipitation it is of importance, too, that, in immunization, the production of the antibodies is effected rapidly and uninterruptedly. Finally, the sediment often produced on keeping the antiserums sometimes simulates a clouding due to precipitates, whether the sediment was not sufficiently centrifugalized before the use of the antiserums or whether some of the centrifugalized sediment was drawn into the pipet, because the high cost of the serums leads one to use them up as far as possible. In order to remove these evils, the following directions are given: (1) Every antiserum (not merely the obviously cloudy ones) is to be centrifugalized as completely as possible. (2) Care is to be used in pipeting. These procedures are facilitated by the recent introduction of tubes having a capillary part at the lower end; in this narrowed part the sediment accumulates and can not be drawn into the pipet even if the pipet touches the bottom of the tube.

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**Blood-Platelet Antiserum, Its Specificity and Rôle in the Experimental Production of Purpura.**

*S. Bedson, J. Path. & Bacteriol., 25:94, Edinburgh, Jan., 1922.*

Bedson has already demonstrated that the red-cell antibody can be removed from an anti-platelet serum, leaving untouched the platelet antibody. By testing this absorbed serum in the animal he wished to  
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obtain a clearer insight into the mechanism of the hemorrhage. One and no tenths c.c. each of anti-platelet serum, anti-red-cell serum, anti-leukocyte serum, antiserum (precipitating) serum and anti-whole-blood serum was injected into 5 guinea-pigs. Blood counts were made before and after inoculation in each case and postmortems performed. Only in the case of an anti-platelet and anti-whole-blood sera was there a drop in the platelet count and only these 2 sera gave rise to purpura in the guinea-pig. Hemorrhages occurred to a greater extent in the former than in the latter sera. Both gave rise to hemagglutination. These tests proved that anti-platelet serum has a specific action when tested in the animal and also that one factor at any rate in the production of the hemorrhage is the removal of the platelet from the circulating blood.

A series of experiments were performed to determine the part played by the hemagglutination in the production of purpura. All the red-cell agglutination was absorbed from the anti-guinea-pig platelet serum without affecting the latter. This was injected into guinea-pigs. It was found that red-cell agglutinin present in anti-platelet serum played no part in the production of the hemorrhages. The action of platelet antibody alone is responsible for the purpura and it is not dependent on any hemagglutination. To test this, a small rabbit was inoculated with 0.75 c.c. anti-rabbit-red-cell serum intravenously. The platelets in the circulating blood of the rabbit were reduced but they gave no rise to purpura. The 2 main factors concerned in the production of the hemorrhages are: (1) toxic action on the endothelium of the vessels; and (2) removal of the platelets from the circulation.

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**The Precipitation of Immune Serums with Acetone.**

*P. Armangué, Rev. españ. de med. y cir., 5:28, Barcelona, Jan., 1922.*

Armangué has worked with serums agglutinating typhoid bacilli and the cholera vibrio. One part of the serum is precipitated with 9 parts of acetone. The mixture is filtered and the precipitate dried in a desiccator. It finally appears as a white powder, which is 11 to 16 times as active as the original serum. From an anti-typhoid horse serum, active in the ratio of 1 to 40,000, a powder was obtained agglutinating bacilli when dissolved in 1:600,000. The agglutination titer of the powder is directly proportional to that of the serum, and inversely proportional to the precipitate obtained from 1 c.c. of the serum. For instance, if a rabbit and horse serum have the same titer of agglutination, the precipitate obtained from the latter (0.062 gm. per 1 c.c. serum) will be more active than that produced from the rabbit serum (0.080 gm. per 1 c.c.). Only a part of the precipitate is soluble in normal saline, but the agglutinin dissolves entirely. The latter also dissolves freely in glycerin, but only in the ratio of from 1% to 5% in 40% alcohol. The powder cannot be preserved, even by protecting it from light and keeping it in the cold. Its agglutinating power is reduced to one-fifth the original, in eight or ten days. Water or glycerin solutions at first deteriorate, but then remain stable. Alcoholic solutions become inactive in a few weeks. Hemolysins may be similarly obtained. They are totally soluble in normal saline, less soluble in glycerin than the agglutinins, and more soluble than the agglutinins in

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40% alcohol. They are less stable than agglutinins. Precipitins and complement fixatives may be also thrown down with acetone, but these properties are not marked in the product obtained. Precipitins have never precipitated antigen in dilutions higher than 1 to 20. Complement fixation is even less intense. By precipitating normal (antigenic) serum, a powder is obtained whose soluble portion is precipitated by the corresponding antiserum. The antigenic powder is 5 to 9 times as active as the serum. A part of the precipitogen seems to be destroyed, or may remain with the insoluble portion. It dissolves 4 times less readily in 40% alcohol or glycerin, than in normal saline. It keeps well. Since the precipitating serums soon alter, the value of the anti-serum must be ascertained for each test.

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### Heterogenic Serum, Age, and Multiplication of Fibroblasts.

*Alexis Carrel and Albert H. Ebeling, J. Exper. Med., 35:17, Jan., 1922.*

The authors have undertaken a study of the relation of rate of growth of a pure culture of fibroblasts and concentration of the medium of heterogenic serum, and the influence of the age of animals from which the serum was taken. The fibroblasts were taken from cultures of a 9 year old strain of chicken connective tissue; serum from dogs and cats was used in the experiments. It was found that heterogenic serum inhibits and prevents the growth of fibroblasts when their concentrations reach certain limits; inhibiting at concentrations of 15-25% and preventing growth about 30%. A relation was found to exist between rate of growth, concentration of serum, and age of animal from which serum was taken.

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### Toxicity of Aqueous Extracts of Animal Organs and Their Neutralization by Serum.

*J. L. Kritschewsky, Biochem. Ztschr., 126:1, Berlin, Dec. 27, 1921.*

In regard to the antitoxic effect which the serum displays against the toxins contained in the aqueous extracts of animal organs, the experiments of Dold have been repeated with a view to checking them.

In the making of the extracts and in mixing them with the serum the numerical proportions of Dold were applied. The serum-mixture and the extracts were kept in a thermostat for two hours. The results of the experiments show that guinea-pigs are more resistant against the toxin in the organ extract than rabbits. The quantity of the mixture of extract and serum that kills rabbits is almost harmless for guinea-pigs half their weight. The neutralizing action of the serum upon the toxin of the organ extracts is not dependent upon the formation of the serum as is the homologous. Also, the foreign serum renders toxin harmless to the same degree. Homologous and foreign sera render only part of their quantity, contained in the weight, harmless. The quantity of the toxin which is fatal in young rabbits is harmless to the adult animal, but if the quantity of the toxin is increased it is fatal to the adult animal also. The rabbit serum retains its property of neutralizing the organ toxin even if it has been inactivated, a fact which is not in accordance with Dold's observations. The same ex-

periments as well as the observations of earlier investigations contradict also Dold's opinion, according to which a difference exists between the clinical symptoms of the guinea-pigs suffering from the effects of the organ-toxic and the anaphylactic shock. Dold mentions, in support of his opinion, that the shock in guinea-pigs resulting from the organ toxin stretches over a longer period (three to twenty minutes) and that no coma takes place. It was found in the above-mentioned experiments that the clinical symptoms of the shock in guinea-pigs after injection of organ extracts is completely identical with the anaphylactic shock. The pathologic-anatomical changes after injection of organ extracts were the same as in anaphylaxis.

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**Studies on X-Ray Effects. IX. The Action of Serum from X-Rayed Animals on Lymphoid Cells in Vitro.**

*James B. Murphy, J. Heng Liu and Ernest Sturm, J. Exper. Med., 35:373, March 1, 1922.*

In the course of an investigation on the biological effects of x-rays, it was noted that while larger doses of this agent destroy lymphoid tissue, very small exposures, after causing a slight amount of destruction, will bring about an actual stimulation of this tissue. With the evidence at hand indicating the indirect action of the x-rays on the lymphoid tissue, it seems of interest to reopen the question and to determine whether or not serum of x-rayed animals has any effect on lymphoid cells in vitro. A number of healthy young rats were exposed to a dose of x-rays governed by the following factors: spark-gap  $2\frac{1}{2}$  in.; milliamperes 10; distance 12 in.; time 14 min. The writers in summarizing say, lymphoid cells, prepared from the thymus and lymph glands of rats, when suspended in the serum of x-rayed rats and incubated for two hours, increase in number from 15 to 30% and mitotic figures are found among these cells in fairly large numbers. A like suspension of cells in normal serum undergoes rapid disintegration and in only one instance among a large number of films examined was a mitotic figure found. The stimulative effect of the serum from x-rayed rats endures from one to two hours after the exposure but is not detectable in the serum taken seventeen hours or later after the treatment. Serum x-rayed in vitro is devoid of stimulative action. The lymphoid cells of rabbits and guinea-pigs are so fragile as to make impossible the obtaining of counts accurate enough for experimental purposes. The serum of one species caused such rapid disintegration of the cells of another that it was impossible to determine the specificity of the reaction.

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**The Determination of Sodium in Serum without the Use of Platinum Dishes.**

*S. J. Wilson, J. Biol. Chem., 50:301, Feb., 1922.*

Wilson reports that in using the method of Kramer and Tisdall for the direct quantitative determination of sodium in small amounts of serum, the sodium need not be precipitated in platinum dishes as these workers suggest. Wilson obtained equally good quantitative results using the so-called tin dishes.

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**A Rapid Colorimetric Method for the Quantitative Determination of the Inorganic Phosphorus in Small Amounts of Serum.**

*Frederick F. Tisdall, J. Biol. Chem., 50:329, Feb., 1922.*

The principle of this method consists in the precipitation of the phosphorus in a trichloracetic acid extract of serum as strychnin phosphomolybdate, the isolation of the precipitate by the use of a centrifuge and small quantities of water, and the subsequent development of a brilliant green color produced by the reduction of the molybdenum present in the precipitate. The reduction is accomplished by the use of potassium ferrocyanid and HCl.

For the precipitation of protein, 1 c.c. of serum is transferred to a 15 c.c. centrifuge tube; to this are added 5 c.c. of a 6% solution of trichloracetic acid, and the two are thoroughly mixed with the aid of a glass rod and allowed to stand for four minutes. It is then centrifuged for four to five minutes at about 1500 r.p.m. and the supernatant fluid poured off. For the precipitation of phosphorus with the strychnin molybdate reagent, 5 c.c. of the supernatant fluid are measured into an ordinary 15 c.c. graduated centrifuge tube, the outside diameter of which is 6 to 7 mm. at the 0.1 c.c. mark. Water is added to bring the volume to 6 c.c. followed by 2 c.c. of the strychnin molybdate reagent which should be added drop by drop, and the tube shaken 3 or 4 times during the procedure. The contents of the tube are then thoroughly mixed by holding the tube at the upper end and tapping the lower end with the finger giving it a circular motion. The contents are allowed to stand for ten minutes during which time they are thoroughly mixed as outlined above. After the ten minutes have elapsed the tube is centrifuged at 1500 r.p.m. for three minutes, the supernatant fluid is poured off and the mouth of the tube wiped with a dry cloth. Three c.c. of water are allowed to run down the sides of the tube which removes any adherent supernatant fluid. The residual supernatant fluid (about 0.1 c.c.) is thoroughly mixed with the added water by tapping the lower end of the tube with the finger giving it a circular motion, while the precipitate is disturbed as little as possible. The mixture is centrifuged for one minute at 1500 r.p.m., the supernatant fluid is poured off and the above procedure repeated, making 2 washings in all. The development of color is accomplished as follows: After the final supernatant fluid has been removed, 2 c.c. of a 1% solution of NaOH are added and the contents mixed with the aid of a glass rod. This causes all the precipitate to go into solution. Water is added to 10 c.c. and the contents are transferred to a 100 c.c. glass-stoppered volumetric flask. Traces of the solution remaining in the centrifuge tube are washed into the flask by means of two lots of 10 c.c. of water, so that the total volume of fluid in the flask is 30 c.c. Then 20 c.c. of a 20% solution of potassium ferrocyanid are added, followed by 10 c.c. of concentrated HCl. The flask is inverted two or three times and allowed to stand ten minutes. Water is added to 100 c.c. the contents are thoroughly mixed, and the color is read in the colorimeter against the standard. The standard is prepared as follows: 1 c.c. of solution of  $\text{KH}_2\text{PO}_4$  containing 5 mg. of P per 100 c.c. [219.3 mg. of  $\text{KH}_2\text{PO}_4$  (Merck) in 1,000 c.c.] is measured into a graduated centrifuge tube, which contains 5 c.c. of water, and the contents are thor-

oughly mixed; 2 c.c. of the strychnin molybdate reagent are then added drop by drop. This step, and the washing of the precipitate and the development of the color, are carried out at the same time and in the same manner with both the standard and the unknown. The amount of precipitate obtained in the standard solution after it is centrifuged is almost exactly 0.1 c.c. of volume. If the amount of precipitate obtained in the unknown is 0.2 c.c. or more, its solution (in 1% NaOH) should be made up to a definite volume in the centrifuge tube and an aliquot taken which would contain approximately 0.1 c.c. of the precipitate. If the amount of precipitate obtained in the unknown is about  $\frac{1}{2}$  the amount in the standard, its solution should be made up to 5 c.c. and transferred to a 50 c.c. volumetric flask with the use of 2 lots of 5 c.c. of water. In all the subsequent steps the volumes used should be halved. When the unknown is made up to 100 c.c. and the standard solution is set at 20 in the colorimeter, the calculation is as follows:  $(20 \div \text{unknown}) \times 6 = \text{mg. P per 100 c.c. of serum}$ . When the unknown is made up to 50 c.c. the result is divided by 2. The strychnin molybdate reagent is prepared as follows: Solution A is made by dissolving 50 gm. of ammonium molybdate in 150 c.c. of warm water. If not clear this solution should be filtered. Solution B consists of 2 volumes of concentrated HNO<sub>3</sub> and 1 volume of water. Solution C is prepared by pouring 1 volume of Solution A into 3 volumes of Solution B. Solution D consists of strychnin nitrate 7.5 gm., water to 500 c.c. The water may be warmed to facilitate solution. One volume of Solution D is poured into 3 volumes of Solution C. This constitutes the strychnin molybdate reagent. The reagent should stand twenty-four hours before it is used. It will keep for at least one month. After the reagent has stood for one or two days a slight precipitate forms which should be filtered off. Two c.c. of the reagent will precipitate 0.2 mg. of P.

The results obtained on serum by this method are accurate to within 5% of the amount of inorganic phosphorus actually present. The presence of Na, K, Ca, Mg, dextrose, urea, uric acid, aceto-acetic acid, creatinin, and creatin in the concentrations found in normal and pathological sera does not interfere with the determination of phosphorus by the technic described.

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On the Determination of Small Quantities of Atropin in Blood-Serum.

J. C. van der Heyde, J. Lab. & Clin. Med., 7:280, Feb., 1922.

In his study of the immunity of the rabbit for atropin, van der Heyde found that a quantitative determination of all alkaloid reagents must first be made. He gives a description of the isolation of the alkaloid out of the chemical mixture called serum, using for this purpose the Stass-Otto method, and adapting it to microchemical analysis. It is stated that quantitative determination of atropin requires 1 c.c. of serum containing maximally 5 mg. alkaline, and the proteids precipitated with absolute alcohol in test-tubes to about 15 c.c., and that the precipitate, when washed several times with alcohol, does not contain sufficient alkaloid to be demonstrated. The alcoholic solution is evaporated, the aqueous solution concentrated to a few cubic centimeters, and a precipitate, consisting principally of fats, is filtered off with a microfilter.

Determination of the quantity of atropin in the solution is made by physiologic methods, color reactions, precipitate reactions, titrimetric methods, and capillary analysis.

In the aqueous solution, the quantity of atropin is determined by the reagent of Mayer, KI.HgI<sub>2</sub>, and the dilution is determined in which this reagent is just able to give a precipitate, from which the atropin can easily be calculated. It is advisable always to make a control determination in addition to the experiment.

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Serologic Investigations with Zeiss' Fluid Interferometer.

*W. Bachmann, Ztschr. f. Immunitätsf. u. exper. Ther., 33:551, Jena, Jan. 19, 1922.*

Changes in the concentration of the serum may be easily ascertained by means of the interferometer. From preliminary experiments, it appeared that one and the same serum shows different values in the course of the day (before and after meals), and that the value determined in regard to any serum is not subject to any changes, if the serum is obtained by sterile methods, and if evaporation is prevented, i.e., that there is no autolysis. The following experiments were carried out in order to examine serologic reactions: Various dilutions of immune serum of typhoid, paratyphoid, and dysentery were mixed with the corresponding bacteria. The interferometer value was determined before and after agglutination (after one hour). The result was decrease of the interferometer value by 9.5°-17° (according to the dilution of the serum) in typhoid, and by 7°-3.5° in paratyphoid, thus indicating flocculation of the immune serum (decrease of concentration) by agglutination. Typhoid immune serum was digested together with extract of typhoid bacilli and with complement for one hour at 37° C., the interferometer value being ascertained before and after complement fixation. The result, increase of the interferometer value by 7°-9°, was interpreted as formation of products of decomposition of the antigen by the ferments of the immune serum. This phenomenon during the first phase of complement fixation may possibly represent the real cause of the modification of the reaction which leads to complement fixation. In the first phase of the Wassermann reaction (serum of patient plus antigen plus complement) and in the Sachs-Georgi reaction, the values were ascertained before and after fixation (continued for two hours). Result: There was a greater increase of the interferometer values during the first than during the second half hour (10°, as compared with 2°), an increase of the values being observed almost without exception in regard to Wassermann-positive serums, whereas no modification was observed in regard to negative serums. It seems, therefore, that during the first phase, the essential factor is the decomposition of antigen, manifesting itself by the increase of the interferometer values; during the further progress, the complement fixation takes place, which is bound to lead to a decrease of the interferometer values. But as the decomposition of the antigen continues, the interference of the 2 processes causes the changes in the interferometer values to be restricted to slight limits.

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**Hydrogen Ion Studies. I. Changes in the Reaction of the Blood During Anaphylactic Shock.**

*Edwin F. Hirsch and J. Lisle Williams, J. Infect. Dis., 30:259, March, 1922.*

From these studies, carried out on the blood of rabbits which had been sensitized by intraperitoneal injections of proteins on three successive days, the authors conclude that there is a diminished alkalinity of the blood during anaphylactic shock, apparently in proportion with the severity of the symptoms. This change in reaction may become so great as to be incompatible with life. The altered reaction of the blood is accompanied by a roughly proportional lowering of the alkali reserve. Slight changes (usually an increase) in the concentration of the sugar of the blood occur in anaphylactic shock, but not to the degree observed in prolonged acidosis.

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**The Specificity of the Desensitized State in Serum Anaphylaxis.**

*Howard T. Karsner and Enrique E. Ecker, J. Infect. Dis., 30:333, March, 1922.*

The specificity of the desensitized state in anaphylaxis has an important practical value. If the occasional hypersensitivity of man to serums which contain specific immune substances could be reduced or eliminated, the safety of their employment would be greater. Since the danger of specific desensitization lies largely in the possibility of severe or even fatal shock, nonspecific desensitization might be of advantage. The experiments here studied were undertaken to study conditions of nonspecific reduction or elimination of anaphylactic shock. The relative effects of different routes of injection in desensitization were investigated, and the type of reaction in shock was observed in relation to the various serums used for desensitization. The authors found that animals sensitized to serum may be desensitized by the use of heterologous serums. The most effective desensitization is by the use of homologous serums. Homologous desensitization is slightly, and heterologous desensitization decidedly, more effective by the intravenous than by the subcutaneous or intraperitoneal routes. Heterologous desensitization develops with apparently the same rapidity as homologous but is of distinctly shorter duration. Reactions appear in intoxicated animals following either form, but are apparently somewhat less severe following the homologous. The latter rule has many exceptions. Heterologous desensitization is more effective than heterologous in protection against large shock doses.

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**Experimental Studies on Anaphylaxis.**

*P. Schmidt and H. Happe, Ztschr. f. Hyg. u. Infektionskrankh., 94:253, Berlin, Dec. 2, 1921.*

With homogenetic serum and agar-agar, Bordet produced anaphylactic states in guinea-pigs, and came to the conclusion that the forma-

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tion of the so-called anaphylatoxin is a physical and not a chemical process. Nathan performed similar experiments with starch anaphylatoxin.

Experiments were performed in which the attempt was made to deprive the agar-agar of its albuminous content, in a manner similar to that already successfully used with starch, without loss of firmness on the part of the agar-agar substances. Following Bordet's method it was always possible to obtain with this agar-agar, which was completely free from albumin, powerful toxins, 2 c.c. of which were capable of producing anaphylactic attacks; a dose of over 2 c.c. killed the experimental animals, after causing typical symptoms. The filtration through a Berkefeld filter like starch anaphylatoxin, demonstrated that the poison was totally eliminated during the brief filtration. When inactivated serum was employed, or when physiologic saline solution was employed instead of serum, no anaphylactic effect was obtained. The agar substance remaining in the fluid poured out after filtering is totally harmless to animals. Atropin and narcosis are unable to prevent the appearance of anaphylaxis. From its action in regard to Berkefeld filtration, it is possible to determine that the agar-agar anaphylatoxin is probably of a corpuscular character. An equal and even a greater part of the filtrate is totally atoxic, while an equal or smaller quantity of the mixture poured off killed the animals. As regards the mechanism of the effect of anaphylatoxin it must be denied that bronchospasm is the primary noxa in shock. A disturbance of the flow in the pulmonic circulation with consecutive edema of the lungs seems to be the more probable noxa.

The safest assumption is of a vascular spasm is probably due to agar anaphylotoxic particles absorbed by the endothelia, which cause congestive disturbances in the pulmonary circulation, and stopping up of the bronchi and vessels. The death of a guinea-pig due to anaphylactic shock is distinctly caused by suffocation; death is not due to heart-failure.

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**Experimental Study of the Mode of Action of Protein Bodies and Irritating Bodies. I. Toxin Fixation and Hypersensitiveness.**

*Döllken and Rudolf Herrger, Münch. med. Wchnschr., 69:185, Feb. 10, 1922.*

From their thorough clinical and experimental study the authors come to the conclusion that the problem of the action of protein bodies is a humoral and a cellular one; that the administration of synergic protein bodies causes about the same reactions of the cells so that their effects may be cumulative. It is not necessary that every component have the same point of action, but one may serve as a pace-maker for the other.

For antagonistic action there is a double mechanism. A mixture of protein bodies and alkaloids prepared cold has a relatively large amount of combining protein body particles, so that the alkaloid is to a certain extent enclosed in a hull and therefore only acts incompletely. The same mixture heated sets free a great part of the protein, and the protein has a very toxic action on a majority of the particles changed by heat; or the protein bodies and alkaloids have such an opposite position with reference to the cell colloids that the point of action is blocked

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for both. In inhibition it is also true that the one substance may serve as a pace-maker for the other. It is essential for the action of an adsorbate that its components should harmonize with one another and with the cells upon which they are to act. The harmonizing is dependent on the quality and quantity of the decomponents, the combining time, the temperature of the mixture, the place and rapidity of injection, and especially on the condition of the cells to be acted upon. If protein bodies are introduced parenterally in the normal organism, the cells of the central nervous system react directly: in animals with sleep; in man with sleep, euphoria and increased efficiency. In other cell groups and centers the reactive capacity to certain stimuli is changed; the threshold of irritation is raised or lowered. In the strychnin reaction of the rabbit the convulsive centers react much more incompletely than normal to the strychnin-protein adsorbate circulating in the organism, but the cells which cause paralysis react very readily. By repeated mechanical stimuli the reactive capacity of the convulsive center can again be brought up to its normal level even when there has been an advanced degree of paralysis. But the cells are in a state of labile balance only with reference to certain stimuli and this is designated as sensitization or hypersensitiveness. But cells of higher and lower centers can by a suitable arrangement of the experiments be made to show the reaction of hypersensitiveness. The phenomenon is related to anaphylactic shock but it is distinguished from it by the fact that minimal doses are not effective and that when blood of the intoxicated animal is injected into another it does not cause the same symptoms. It is also closely related to focal reactions of diseased organs to non-specific albumin.

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### **Anaphylaxis in Excised Organs of the Frog.**

*M. Kochmann and P. Schmidt, Klin. Wchnschr., 1:222, Berlin, Jan. 28, 1922.*

The experiments of the authors contradict the findings of Arnoldi and Leschke, who assert that they demonstrated sessile receptors in the organs of frogs, and that on passing an artificial circulation through the hind legs of previously treated frogs, they observed dilatation of the vessels after injection of human serum and also after injection of anaphylatoxin. In the authors' experiments, they always found contraction of the vessels after the injection of either serum or anaphylatoxin. The excised intestine reacted in the same way to anaphylatoxic and normal serum, as did the excised muscle and nerve of a nerve-muscle preparation. Therefore the authors deny the presence of sessile receptors in the frog and also the presence of dissolved toxic substances in anaphylatoxic serums.

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### **Researches on Parabiosis, with Special Reference to Transplantation and Hypernephrectomy.**

*Tomosuke Mayeda, Deutsch. Ztschr. f. Chir., 167:295, Leipzig, Dec., 1921.*

Parabiosis is an excellent means of studying various phenomena of intoxication and immunization, as well as the processes taking place during transplantation. White rats have been found the best animals  
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for surgical union. The operation consists in establishing a communication between the abdominal cavities of both test animals, by cutting through the abdominal parieties and uniting the wound edges of the two animals by an exact suture; it is necessary to establish broad union of the cut tissues. The animals so united may die of the shock of the operation, of wound infection, or of peritonitis. Parabiotic animals do not develop as well as the normal, since they disturb each other when eating and sleeping. If they have survived the first five weeks, they can, as a rule, go on and develop. The most frequent cause of death in parabiotic animals is an increasing anemia and failure of growth in one animal, the other showing normal or excess development. Sharp distinction must be drawn between pairs of animals exhibiting this unfavorable biologic condition and those which do not. Mayeda calls the first group heterogeneous parabiosis, while to the latter group he applies the name homogeneous parabiosis. In homogeneous parabiosis both animals heal after the union, as would a wound in a single animal. The most important sign of heterogeneous parabiosis is the fact that two to five weeks after the operation one partner becomes pale, showing a definite line of demarkation from the other; this progresses, and the animal succumbs after one or two weeks.

The author looks to a property of the blood as the cause of heterogeneous parabiosis. Iso-agglutinin and isoagglutinins are the only injurious factors known to be active between 2 animals of the same species. They are never encountered between the partners of homogeneous parabiosis, the erythrocytes of the stronger partner are not affected by the serum of the weaker. The serum of the stronger produces slight hemolysis, but no agglutination of the red cells of the weaker partner. An uninterrupted interchange of blood takes place between the partners of parabiosis. It may therefore be assumed that iso-agglutinins and isoagglutinins are produced and constantly carried to the other partner, whose erythrocytes are thus gradually destroyed. But with the interchange of blood between the 2 animals, iso-agglutinin and isolsin do not always appear. Isolsin is not the only cause of heterogeneous parabiosis, which depends upon an antagonism in a broader sense, of one animal for another.

Thus, parabiosis is a special form of homeoplasty, one entire animal representing the transplant. When the parabiosis is heterogeneous, it is unsuccessful, while homogeneous parabiosis represents a successful transplant. In heterogeneous parabiosis the wound will not show any tendency to heal for weeks; histologically, a band of granulation tissue forms a line of demarkation between the two animals. In parabiotic animals there exists direct communication of the circulatory apparatus by means of a capillary system; in heterogeneous parabiosis this capillary system is poorly developed. Soon after the operation, communication is established through the lymphatic system, and this persists. In nonparabiotic animals, skin autoplasty is almost always successful; homeoplasty is more difficult, especially in animals not related. Animals in whom a previous skin homeoplasty is successful, are much better suited for parabiotic operations than those in which it fails. Parabiosis does not render skin homeoplasty between partners easier; autoplasty is almost out of the question in parabiotic animals, because parabiosis is an artificial condition against which the body mobilizes all its protective forces. If, however, the parabiotic animals are separated in such a

fashion as to leave a skin and muscle flap of one animal in contact with the other, the flap will unite in case of homogeneous parabiosis, because it has previously been supplied with blood by the partner. In heterogeneous parabiosis the flap becomes acutely necrotic. Pedunculated homeoplasty shows poor results in parabiotic animals. Transplantation of the adrenals in such animals was almost always unsuccessful. Bony transplants in such subjects usually behave as they do in normals. Bone transplanted by autoplasty, as well as by homeoplasty, is gradually replaced by newformed tissue.

One partner of homogeneous parabiosis can without danger be deprived of both adrenals; this cannot be done in heterogeneous parabiosis. If the partners of homogenous parabiosis are separated about four weeks after a bilateral hypernephrectomy has been performed in 1, this one can survive without adrenals, since its accessory adrenals have become hypertrophied. If the partners are not severed, the adrenals may, after the same time, be removed from the second partner and hypertrophy of the accessory adrenals will compensate for the loss.

In heterogeneous parabiosis the blood-injuries early produce a state of irritation in the bone marrow of the lesser partner; this may be followed by degeneration of the marrow and of the spleen, myelogenous foci developing in the latter organ.

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**Cutaneous Blood (So-Called Capillary Blood).**

*Christen Lundsgaard and Eggert Möller, Ugeskr. f. Læger., 84:167, Copenhagen, Feb. 9, 1922.*

It is of importance for the study of a series of pathologic and physiologic problems to know the composition of the cutaneous blood and particularly its relation to arterial blood. As a criterion for the composition of the blood Lundsgaard and Möller chose the oxygen, partly because the oxygen contents of the blood usually undergo a change in the capillary vessels, partly because the maximum quantity of oxygen in contradistinction to that of all the other components can be ascertained, as it corresponds to the sum of capacity of hemoglobin for binding the oxygen and the quantity physically dissolved. The specimens of blood were taken by puncture of artery (in 1 case), and puncture of vein; the cutaneous blood was taken by making with a sharp knife 1 to 3 cuts ( $1\frac{1}{2}$  cm. long,  $\frac{1}{4}$  cm. deep) in a finger pulpa; the blood was made to run into a bowl containing a sufficient quantity of liquid paraffin, with some pulverized oxalate of potash in order to prevent coagulation of the blood. As a rule, 3-4 c.c. blood was obtained. For the analysis of the oxygen contents of the blood, van Slyke's method was used. The experiments were made on (1) normal individuals in repose; (2) normal individuals after efforts; (3) individual in repose, suffering from left side exudative pleuritis; (4) individual suffering from emphysema of the lungs, bronchial asthma and chronic bronchitis in repose after effort; (5) normal individual while respiring air containing little oxygen. In all these cases, the cutaneous blood proved to be practically identical (96.6% maximum capacity) with the arterial (97.5%) blood, whereas the venous blood proved to have only 75%; it will, therefore, be possible in many cases, to get practically the same information from cutaneous as from arterial blood. There is every

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reason to believe that the cutaneous blood comes essentially from the arterial parts of the cut capillaries, probably due to the tendency of the severed veins to close. The identity as to oxygen shown by these experiments extends to other components (salt, sugar).

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**Studies in the Regeneration of Blood.**

*Zalia Jencks, Am. J. Physiol., 59:240, Feb. 1, 1922.*

In Jencks' studies in the regeneration of blood, the preliminary experiments were designed to discover the limit of successful bleedings in the rat, the period for regeneration of blood after hemorrhages, and the effect of the dietary factors on such regeneration. In the early experiments, the rats were bled from incisions made in the tail but later this procedure was abandoned and the blood in the desired quantity (from  $\frac{1}{3}$  to  $\frac{1}{2}$  of the estimated total) was secured via a slit in the jugular vein of the anesthetized animal. Careful examination of the blood for erythrocytes and percentage of hemoglobin was made prior to the bleeding of the animals. In judging regeneration the return of the number of red blood corpuscles and the percentage of hemoglobin to the preliminary values were the criteria. The tabulated results show that hemorrhages of approximately one-third of the estimated total blood volume can be borne by albino rats without interfering with complete recovery. When one-half or more of the blood was removed by hemorrhage, death ensued. By varying the diet from elimination of all but 1 factor therein, the speed of regeneration of blood was changed, but with each diet the organism replenished its normal supply of blood to the original values for red cells and hemoglobin. Protein permitted more rapid blood regeneration than either carbohydrate or fat when fed as a sole nutrient (2.0 gm. daily). The diets of vitamin-rich food, even in very small amounts, gave somewhat more speedy regeneration than any other diet containing 1 food factor only.

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**Chemical Blood Analysis. IV. Calcination Methods.**

*M. Richter-Quittner, Biochem. Ztschr., 126:97, Berlin, Dec. 27, 1921.*

In order to analyze the electrolytes and nonelectrolytes of the blood, one may remove the organic material either by deproteinization, by ultrafiltration, or by calcination. The latter method is employed in the determination of the mineral components present in organic fixation. The determinations of the entire content of potassium and of calcium, in particular, require this method. Since potassium and calcium in the blood are partly bound to the albumin, the combustion methods are apt to furnish biologically correct results. Of the inorganic components, the total phosphorous content is usually determined by means of the acid mixture method of Neumann, the chlorin according to Koranyi, the total phosphorus, the iron, the total potassium and the total calcium, by calcination. If it is intended to determine the mineral components of the blood by a single analysis, the determination of the lowering of the freezing point, of the conductivity and of the total ash is the proper method. The first 2 procedures, however, are probably inapplicable, if

colloidal systems are concerned. As regards the total ash determination, one must remember that it involves an entire series of chemical transformations; consequently, a blood ash must have a different chemical composition and thus, also, a different weight, according to the temperature at which the calcination was carried out. The analysis of the glowing ash does not, therefore, always give a correct idea of the inorganic components of the blood, either as regards the state or as regards the quantity in which they were present primarily. So far, the experiments showed that the human blood corpuscles contain, under normal conditions, very little inorganic substance, in particular no chlorine, no calcium, no sodium, and that the plasma possesses a far higher concentration of mineral substances than do the blood-corpuscles. The physical equilibrium is not controlled by osmotic pressure, but by the swelling pressure of the colloids. The higher the concentration of the colloids, the greater, of course, is the swelling pressure.

The procedure of calcination was as follows: 10 c.c. blood were defibrinated, or their coagulation prevented by means of hirudin. Then the blood was transferred into a weighed platinum dish, dried over the water bath, and calcined over a small flame. The residue was washed with hot water, the filter residue and the filter were returned to the platinum dish, and calcined again. These washings were repeated 8 times. Finally, all the filtrates were combined, dried over the water bath, and carefully brought to red heat over a small flame and maintained until it became constant. The results confirm the fact that the method of calcination is not suitable for the study of the physical equilibrium existing between blood-corpuscles and plasma, but that it is indispensable in the determination of the total potassium, the phosphorus and the iron. Under physiologic as well as pathologic conditions, the blood-corpuscles contain less mineral substances than the corresponding serum and, under the influence of nervous stasis, give off additional mineral substances to the serum.

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**Calcium Content of the Blood and Effect of Different Toxins on It.**

*Ernst Billigheimer, Klin. Wochenschr., 1:256, Berlin, Feb. 4, 1922.*

Following up the work of Meyer, Loewi and others, Billigheimer tested the rôle of calcium in increased irritability of the vegetative nervous system and also in the irritation of this system by certain drugs. In his experiments on about 70 normal and pathologic individuals, he found that in normal individuals the calcium content of the blood was very constant, the variations being only from 9.2 to 9.6 mg. per cent. Values above or below this may be regarded as abnormal. After a period of a diet poor in calcium, the calcium values were a little higher than after a few days on a diet rich in calcium.

On testing with adrenalin, Billigheimer found in 13 out of 15 cases that the calcium content of the blood decreased. In only 2 cases was there a slight rise, and this was where the pulse and blood reactions were slight, where there was no general reaction at all. Therefore, the varying degrees of decrease in the calcium content after adrenalin is an expression of the degree of stimulation of the sympathetic by adre-

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nalin. This fall in the calcium content is independent of changes in concentration of the blood.

To test the calcium content in stimulation of the vagus, experiments were made with pilocarpin. These showed a rise in calcium content, but the author thinks it is questionable to what degree this change was due to the increased concentration of the blood. After atropin, the calcium content fell slightly, which is in harmony with the hypothesis that the effect of atropin injection corresponds to a weakened adrenalin action. With Elias' theory in mind, Billigheimer tested the action of primary and secondary sodium phosphate. The calcium content decreased and the higher the dose, the greater the decrease. There was no subjective or objective effect on the patient. But the serum albumin content decreased more or less in every case. As there was not an absolute decrease in the serum albumin content, but only a withdrawal of fluid from the tissues, the author thinks there was probably in these cases only an apparent decrease of calcium. In conclusion he thinks it probable that stimulation of the sympathetic by adrenalin is due to an increased splitting off of calcium ions at the nerve endings which bring about decrease of calcium in the blood.

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**The Hydrogen Ion Concentration and Bicarbonate Level of the Blood in Pneumonia.**

*A. L. Barach, J. H. Means, and M. N. Woodwell, J. Biol. Chem., 50:413, Feb., 1922.*

A method of finding the acid-base equilibrium in disease, consists in the determination of the carbon dioxid dissociation (or absorption) curve, and the carbon dioxid content of the patient's arterial and venous blood, and from these data the construction of the carbon dioxid diagram of Haggard and Henderson. The further studies reported in this paper were carried out in the same manner, except that the van Slyke blood-gas apparatus was used instead of the Henderson. The combined method of van Slyke and Statie was used. In this research, all arterial or A-points, and all venous or V-points, were placed on the dissociation curve at its intersection with the abscissa representing the carbon dioxid content of the blood as found by analysis. The curves plotted represent blood equilibrated with air and various tensions of carbon dioxid at the patient's body temperature. The patients were all suffering from pneumonia. From the tabulated results, the authors observed that the alkali of the blood in pneumonia, as shown by the level of the carbon dioxid capacity at a fixed carbon dioxid tension (40 mm.), was found to be sometimes within normal limits, sometimes somewhat below normal limits. The average in the pneumonia group was 43.2 volumes per cent. The arterial pH in pneumonia as calculated from the carbon dioxid diagram and corrected for oxygen unsaturation and body temperature showed an average of 7.31. No relation could be found between pH or dissociation curve level and degree of anoxemia or prognosis. It is suggested that in pneumonia patients showing acidosis either in the sense of a low level of available blood alkali or of decrease in pH or combination of the two, the administration of sodium bicarbonate may be helpful in diminishing the work of the respiratory bellows. By such a procedure a pH less alkaline than normal may be brought to

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normal with no increase in ventilation because of a raising in the level of the dissociation curve. Or in a case with low curve but normal pH to start with, the raising of the curve may diminish the amount of ventilation necessary. The use of sodium bicarbonate should be carefully controlled, however, to avoid the production of alkalosis, and when anoxemia is present should be combined with oxygen therapy.

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**The Relations of Carbon Dioxid in Acidified Blood.**

*T. R. Parsons and Winifred Parsons, J. Physiol., 56:1, London, Feb. 14, 1922.*

Previous workers have shown that as the hydrogen-ion concentration of a solution containing hemoglobin is increased, say by means of carbonic acid, at a certain value of pH which is on the alkaline side of the iso-electric point of hemoglobin there is a sudden increase in the quantity of carbon dioxid taken up by the solution, while the reaction, as judged by the course of the carbon-dioxid dissociation curve, remains constant. Over this range of constant pH a whole extra molecule of carbon dioxid is taken up for each molecule of hemoglobin present. Direct measurements of the pH over this range have shown that a probable explanation is that each hemoglobin molecule is giving off a single atom of available sodium to form sodium bicarbonate with the extra carbon dioxid. Other workers have found evidence of the combination of a second similar extra molecule of carbon dioxid at a more acid reaction. The present writers believe that if the extra carbon dioxid is combined directly with the hemoglobin in a nonionizing compound, it must all be confined to the corpuscles, while if it is combined as sodium bicarbonate, then this salt (first formed in the corpuscles according to the authors' theory) will distribute itself between the 2 phases by diffusion and ionic interchange. The concentrations of sodium bicarbonate outside and inside the corpuscular membrane will not necessarily be equal, but one can be certain that at least that portion of the extra carbon dioxid which is found in the plasma cannot be combined with the hemoglobin, but is probably in the form of sodium bicarbonate. To obtain evidence on this point the authors performed a series of experiments. Human blood acidified by the addition of a small amount of lactic acid, was saturated with gas mixtures containing various tensions of carbon dioxid. The plasma was separated without loss of gas and its carbon dioxid content estimated. The experiments were carried out at different temperatures and the results tabulated in the article. From a study of these graphs one notes that there are 4 sudden inflections in the carbon-dioxid dissociation curve of the true plasma of acidified oxygenated blood. At a temperature of 15°C. these occur at pH of 6.88, 6.73, 6.61 and 6.48 respectively; at 38°C. the pH at which the first inflection occurs is 6.61. The first two of these inflections may probably be explained as due to the formation of sodium bicarbonate from sodium obtained from the oxyhemoglobin molecule; the remaining inflections may be due to a similar formation of sodium bicarbonate, or to the formation of a bicarbonate of oxyhemoglobin. But if such an oxyhemoglobin bicarbonate is formed it must necessarily undergo ionization in solution. The constancy of the reaction during these inflections is due to the fact that the oxyhemoglobin is in the pre-

cipitated condition. Oxyhemoglobin forms a separate phase in a reacting system when it is in the precipitated condition, but not when it is in colloidal solution. Hemoglobin is to be regarded as a polyvalent colloidal amphotyte capable of giving rise to ions of various valencies in solution. The authors suggest that the oxygen-combining power of hemoglobin is determined by the ionic charge it carries.

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**The State of the Carbon Dioxid in the Blood.**

*T. R. Parsons and Winifred Parsons, Biochem. Ztschr., 126:109, Berlin, Dec. 27, 1921.*

Zuntz and Löwy formulated the theory that under physiologic conditions some of the proteins of the blood are capable of forming acids of sufficient strength to liberate  $\text{CO}_2$  from sodium bicarbonate, thus giving rise to sodium proteinate and playing an important rôle in the transportation of  $\text{CO}_2$  by the blood. The hemoglobin, as well as the  $\text{CO}_2$ , are weak acids in the blood, among which the active or reserve bases of the blood are distributed according to their relative strength and concentration. The oxyhemoglobin is a stronger acid than the reduced hemoglobin. It follows from the theory of the amphoteric electrolytes that the acid strength of any amphotyte at a value located on the alkaline side of the iso-electric point does not depend upon the difference between these 2 pH values, but only upon the acid dissociation constant of the individual substances. According to Michaelis, the acid ( $K_a$ ) or base ( $K_b$ ) dissociation constant of an amphotyte is related to its iso-electric point ( $J$ ) in such a manner that the following formula holds:  $1 = \text{square root of } (K_a \cdot K_b) \text{ times } K_w$ .

In this formula  $K_w$  is the dissociation constant of water. From this formula it is evident that only the relation and not the actual values of  $K_a$  and  $K_b$  determine the value of  $J$ . This may be expressed thus: The acid strength of an amphotyte, at a given pH, may be greater than that of another amphotyte, even if the iso-electric point of the first amphotyte lies nearer the alkaline region than the iso-electric point of the latter amphotyte. Experiments on the saturation of the blood with  $\text{CO}_2$  have shown that the maximum quantity of this gas capable of being assimilated by the blood corresponds to a concentration of bound carbonic acid of about 0.045 gram-molecules per liter. The maximum capacity of normal blood for binding oxygen corresponds to approximately 18.5 c.c. per 100 c.c., i. e.,  $18.5 \div (22 \text{ times } 4 \text{ times } 10^{-3})$ , or 0.0083 molecules per liter. Since the hemoglobin molecule reacts with one molecule oxygen it follows that 0.0083 is also the molecular concentration of hemoglobin in the normal blood. Consequently, if the hemoglobin effects in any way the binding of the  $\text{CO}_2$ , the molecule hemoglobin must be capable of binding  $0.0083 \div 0.045$ , i. e., about 5 molecules  $\text{CO}_2$ . If this  $\text{CO}_2$  combines completely with the sodium derived from the hemoglobin, the assumption suggests itself, that the hemoglobin is a 5 basic acid.

Direct determinations of the hydrogen-ion concentration have shown that the  $\text{CO}_2$  introduced does not directly combine with the hemoglobin but that the hemoglobin probably gives off one atom Na which combines with the  $\text{CO}_2$  to form sodium carbonate.

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Blood Fermentation Values. I. The Quantitative Estimation of Catalase, Protease, Peroxidase and Esterase in a Drop of Blood.

A. Bach and Sophie Zubkowa, *Biochem. Ztschr.*, 125:283, Dec. 18, 1921.

An intimate relationship exists between the condition of the living organism and the activity of its organic and cellular ferments, and the recognition of this fact is of immense importance in pathology and physiology. This recognition may be gained if the characteristic fermentation value for each of the blood ferments can be determined. The quantitative methods of estimation devised for the 4 blood ferments—catalase, protease, peroxidase and esterase—are here described. These, as well as the control tests, require only 0.006 c.c. blood, and are accomplished with ease in a few hours. The values arrived at are relative. A drop of blood is drawn into a 20 c.c. capillary pipet up to the mark and is transferred to a little flask containing 20 c.c. distilled water. Of the blood solution so obtained, 1 c.c., corresponding to 0.001 c.c. blood, is employed for each estimation. In the course of the investigation it was found that the estimation of catalase and protease is best when they are combined in the following manner: Three Erlenmeyer flasks, *a*, *b*, *c*, each receive 7 c.c. water; *a*, receives 1 c.c. boiled blood solution; *b* and *c* each receive 1 c.c. active blood solution; *a* and *b* are allowed to stand one hour at 17°C., *c*, one hour at 37°C.; *c* is then allowed to cool down to 17°. To each flask 2 c.c. of hydrogen peroxid 1% is added, the flasks are allowed to stand another half-hour, each is acidified with 3 c.c. sulphuric acid 10% and titrated with tenth-normal potassium permanganate until a pink color is obtained. The difference between *a* and *b*, reduced to cubic centimeters of hydrogen peroxid, is the amount of hydrogen peroxid that is decomposed by 1 c.c. active blood solution at 17°. The difference between *a* and *b* shows the amount of peroxid decomposed by the active blood solution kept at 37°. The difference between the amount of hydrogen peroxid decomposed at 17° and that decomposed at 37° shows, in milligrams of hydrogen peroxid, the diminution of the action of catalase under the influence of protease (protease value). The two values are defined thus: The catalase value is the amount of peroxid, expressed in milligrams of hydrogen peroxid, that is decomposed, under the conditions described, by 0.001 c.c. blood. The protease value is the diminution of the action of catalase, expressed in milligrams of hydrogen peroxid, produced by the previous warming of the blood solution to 37°. The catalase value varies from 14 to 18, the protease value from 3 to 5. Peroxidase is a far more sensitive catalyzer than hemoglobin, so that whereas in undiluted blood the peroxidase reaction is concealed, in diluted blood it comes to light and can be estimated quantitatively. For this purpose 1 c.c. blood solution, 10 c.c. water, 1 c.c. guaiacol 1%, and 1 c.c. hydrogen peroxid 1% are put in a narrow test tube. The mixture is allowed to stand half-an-hour at room temperature, after which the color produced is compared in the colorimeter with the scale described herewith. The latter consists of several sealed tubes, each of which contains 10 c.c. of a liquid for comparison, in increasing concentrations. As oxidized guaiacol is unstable the following liquid was employed for the scale: 10 gm. egg-albumin, 5 gm. sodium carbonate and 2 gm. cobalt nitrate in 250 c.c.

water. These were boiled for one half-hour and filtered through asbestos. Ten dilutions of this reddish-brown liquid were prepared, of which the one colored least corresponds to about 0.05 mg. fully oxidized guaiacol in 10 c.c. oxidized liquid. The amount of guaiacol, expressed in thousandths of a milligram, that is oxidized by 0.001 c.c. blood, with the help of peroxid, is the peroxidase value of the blood. It varies from 50 to 100. The estimation of esterase was effected by employing 1 c.c. blood solution (1:1000), 2 c.c. water, 5 c.c. freshly prepared thiocol solution 4% (potassium guaiacol sulphonic acid), 1 c.c. dilute peroxidase solution and 1 c.c. hydrogen peroxid solution. A control test was carried out under the same conditions with boiled blood solution. After allowing to stand one half-hour, at room temperature, the guaiacol that has been split off and oxidized is estimated colorimetrically in the manner described for the estimation of peroxidase. The oxidizing agent (peroxidase plus hydrogen peroxid) is added to the blood solution. The amount of guaiacol, expressed in thousandths of milligrams, which is split off by 0.001 c.c. blood from the guaiacol ester, is termed the esterase value of the blood. The esterase value varies in apparently healthy human beings from about 50 to 100. Like peroxidase, esterase is not sensitive to an increase of temperature from 17° to 37°. The method is, therefore, based on the fact that the oxidation system in question rapidly attacks free phenols but does not attack phenol esters.

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**Experiments on the Fermentative Characteristics of the Blood. V. The Appearance, in the Blood, of Ferments in Various Experimental Conditions.**

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*Ludwig Pincussen, Biochem. Ztschr., 126:93, Berlin, Dec. 27, 1921.*

The so-called defensive ferments of Abderhalden, which are found under given conditions in the blood, are derived, so far as the specific enzymes in the blood are concerned, from organ cells. The increased appearance of enzymes in diseases is due to an increased disintegration of the cells of the affected organs. For this reason, the diagnosis of carcinoma by the aid of Abderhalden's method meets with difficulties, inasmuch as we cannot except to find specific enzymes directed against the tumor albumin until the tumor cells are already broken down. There is no such formation of enzymes in the beginning of the development of cancer.

Transplantations are undertaken in order to furnish experimental proof of this theory of the appearance of enzymes in the blood. The experiments proved that it was impossible to verify the theory mentioned above. Since, according to the experiments of Heilner and Petri, resorption of the endogenous albumin may result in the appearance of ferment in the blood, the kidneys of rabbits were injured in various ways, and then serum was used in the search for ferments against the kidneys. Physiologic saline solution was injected, later on also NaOH, which resulted in severe hemorrhagic nephritis. The animal died. Serum taken from these animals after six hours effectively broke down liver and kidney, while the serum of untreated animals had no such effect. These experiments, therefore, exhibited a specificity of the cell ferment in accordance with the theory. On account of the insufficient nutrition of the kidneys, cells are destroyed, their ferments

enter the blood, and are found there. In experiments in which the kidneys were removed it was impossible to demonstrate enzymes conclusively. The same is true for experiments in which a wedge-like piece was cut out of the kidney and transferred to the peritoneal cavity, while the kidney wound was sutured. An injury of the kidney by producing an uraniumnephritis, however, produced a considerable increase in the destruction of the serum of the treated animal.

Although the conditions are still complicated in many cases, every case shows that in the absence of complications specific organic ferments are actually entering the blood and may be demonstrated there by their strictly specific catabolic ability.

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**The Distribution of the Blood Sugar in the Circulating Blood.**  
*Ladislaus Csaki, Wien. Arch. f. inn. Med., 3:459, Jan. 20, 1922.*

Blood sugar is determined by the method of Bang from the general blood stream taken from the vein of the finger and determined from the plasma. Up to now, the authors have always defibrinated the blood or prevented the clotting by various means. Csaki believed that the red blood cells were injured by these methods and he obtained the plasma in the following way: 5 c.c. of blood was taken from the vein and immediately centrifuged in a corked B centrifuge tube. This led to immediate separation of the plasma and he could then place it in the paper. The per cent. volume of the red blood cells was determined by Hedlin's hemocrite method. Results: either no, or else very minimal, quantities of sugar could be demonstrated in the red blood cells of nondiabetics, even when there was an alimentary hyperglycemia. Considerable sugar was found in the red cells of diabetics regardless of whether there was hyperglycemia or not.

Normal blood which is defibrinated, or which is treated with substances retarding clotting, reacts like the blood of a diabetic. A considerable part of the blood sugar was found in the red blood cells. The following hypothesis is based on these findings: Normal erythrocytes are impermeable to sugar and take up as much sugar as can be used up within them but no more. This is why there were traces of sugar. The cells become permeable to sugar in diabetics, but they cannot change the sugar or use it all and this leads to an accumulation of sugar in the red cells. It is possible that the cells of other organs react to sugar in the same way as do the red blood cells.

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**Catalase Content of the Blood and Its Significance for Differential Diagnosis.**

*E. Segall and M. Händel, Deutsch. Arch. f. klin. Med., 138:243, Leipsic, Jan. 24, 1922.*

In the main, the authors employed van Thienen's permanganate method; but they caused the reaction to take place in the incubator at 37°C. They placed 50 c.c. blood with 50 c.c. physiologic solution of NaCl into retorts and kept 10 c.c. of this, with 30 c.c. of a 1% solution of H<sub>2</sub>O<sub>2</sub>, in the incubator for two hours. After the addition of H<sub>2</sub>SO<sub>4</sub> (50%), 5 c.c. were titrated with permanganate solution containing 3.7195 gm. KMnO<sub>4</sub> per liter. The erythrocytes are the principal factor

in the decomposition of  $H_2O_2$  by the blood. But urea, even in a concentration of 0.04%, checks this action. The rest-nitrogen content of the serum is approximately 0.3%. Fibrin or fragments of tissue will increase the effect. Cl ions also have a slightly adjuvant effect. The catalase values, as determined by the 2 authors, are smaller than those found by van Thienen, probably due to the food situation in Austria. In various diseases, especially in cachexia, there is a decrease in the catalase content. The same is the case in anemia, even in the absence of cachexia, especially in pernicious anemia. Van Thienen sometimes found the catalase index increased in pernicious anemia.

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**The Chemical Nature and Changes of Blood Fat.**

*I. Lifschütz, Hoppe-Seyler's Ztschr. f. physiol. Chem., 117:212, Berlin, Dec. 27, 1921.*

Various kinds of bovine blood were examined for the composition of the blood fat. From the comparative results the following conclusions are drawn: With increased oxidation (black) of fat in the blood the amount of glycerin fat is greatly diminished, while cholesterin is largely increased. Amorphous cholesterin forms a much larger proportion (40%) of the largely increased unsaponifiable part (50%) of the strongly oxidized blood fat, than the strongly oxidized crystalline cholesterin (60%). These conditions are reversed in the case of fat oxidized only to red-brown, in which crystalline cholesterin is 7 times greater than amorphous cholesterin. On the strength of his observation that fat rich in cholesterin is poorer in unsaturated oleic acid, and that fats richest in cholesterin (blood fat, wool fat) are subject to the strongest oxidization, the author asserts that oleic acid is the mother substance of cholesterin and that the latter owes its origin to the oxidative decomposition of oleic acid.

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**Is Gabbe's Glycerin Reaction an Indicator of the Lipoid Content of the Blood after an Injection of Exogenous Substances.**

*Bruno Engelmann, Münch. med. Wchnschr., 69:120, Jan. 27, 1922.*

Gabbe says that after an injection of exogenous substances the lipoid content of the blood is changed. To determine this change he made the following test: 0.5 c.c. of fresh active serum are covered with 0.5 c.c. of glycerin solution and are allowed to remain in an incubator for twenty-four hours at 37° C. A positive reaction is indicated by turbidity of the upper layer. Intravenous injections of exogenous substances, in doses which do not cause fever, are said to increase the reaction, or even to transform a negative reaction into a positive one. Injections accompanied by fever are said to have weakened the reaction and caused the transformation of a previously positive reaction into a negative one. This test would permit the control of the therapeutic effect of substances recommended for use in stimulation therapy and to determine the proper doses. Experiments undertaken in this direction gave the following results: After meals which contained 30-50 gm. fat, the serum became turbid, when covered with glycerin it produced a distinct ring at the outer zone,

In fatless nutrition an injection of exogenous substances hardly ever produces a positive glycerin reaction. This is a positive indication that the glycerin reaction is connected with the absorption of fat and, therefore, cannot be considered as an indicator of the lipoid content of the serum.

The test by covering the serum with a 5% solution of glycerin, therefore, is not suitable for determining the proper dosage.

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(1e—350)

Takayama's Method of Preparation of Hemochromogen-Crystals.

*Georg Strassmann, Münch. med. Wchnschr., 69:116, Jan. 27, 1922.*

The old method of preparing hemochromogen crystals (addition of pyridin and ammonium sulphid, or hydrazin hydrate, to the blood-particles which are to be examined) has the disadvantage that the crystals do not keep well.

Strassmann recommended 2 reagents for the preparation of hemochromogen crystals for forensic identification of blood, which seem to have many advantages over all other substances. The first reagent, which keeps for a very long time, is composed of 5 c.c. of a 10% grape-sugar solution, 10 c.c. of a 10% sodium hydroxid solution, 65 c.c. of distilled water, and 20 c.c. of pyridin. A few drops of this solution are added to the blood-particles placed upon an object-glass, and the mixture is heated very carefully over a small flame, until the blood-particles, which are of a greenish color, turn pink. Within a few minutes hemochromogen crystals are formed; their number increases constantly, and they maintain their shape for several days without the addition of any preservative substance. By carefully covering them with Canada balsam one may keep them for several weeks.

The second reagent is still more effective, and is composed of a 10% sodium hydroxid solution, 3 gm. pyridin and 3 gm. grape-sugar, and 7 c.c. distilled water. Abundant formation of crystals takes place without the necessity of heating. With old blood about twenty minutes, or even more, are required before any crystals are formed. This reagent deteriorates after two or three weeks, and must be renewed.

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(1e—351)

Hemolysis of Erythrocytes in Contact with Glass.

*Wallace O. Fenn, J. Exper. Med., 35:271, Feb., 1922.*

In the course of some experiments in which counts of red corpuscles were made without fixatives, the author observed hemolysis when the corpuscles came in contact with the glass. He undertook a study of the conditions and cause. He found that washed erythrocytes hemolyze readily in contact with glass, especially if it is soiled, even when it is coated with paraffin, paraffin oil, vaselin, and also on mica surfaces. The presence of 0.1% serum inhibits such contact hemolysis. The erythrocytes are more adherent than normally in acid solutions.

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**The Diagnostic Value of Schilling's Blood Picture.**

*Emmerich Haynal, Wien. Arch. f. inn. Med., 3:507, Jan. 20, 1922.*

Schilling's method of counting the white blood-cells has proved its value. The advantage of Schilling's method is in the fact that one may gain a good insight as to the shifting of the nucleus of the neutrophils. This requires only a little more work than is needed for a qualitative determination and it is not necessary to study each nucleus minutely.

(1) Chronic infections (syphilis, tuberculosis, malaria). Normal leukocyte count, increase of the red nucleus, absence of myelocytes and metamyelocytes. There is apparently a hindrance to the development of the neutrophils.

(2) Leukopenia: No shifting of the nuclei if cachexia is the cause, as in typhoid or paratyphoid. There is always shifting of the nuclei even to myelocytes in lesions of the bone-marrow resulting from sepsis and peritonitis.

(3) Leukocytosis resulting from benign affections, as angina or bronchitis, produces a mild shifting of the nuclei without myelocytes or metamyelocytes. Severe infections cause shifting of the nuclei to metamyelocytes.

(4) Regenerative shifting to myelocytes occurs in septic, purulent processes.

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**1f. PATHOLOGY.**

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**Cleft Palate in Animals.**

*Frederick Hobday, Proc. Roy. Soc. Med., (Pathol. Sect.), 15:3, London, Feb., 1922.*

Veterinarians are fairly well agreed that cleft palate is a hereditary defect due to too close inbreeding. It is especially frequent in well-bred animals, and with these inbreeding is the custom. Operation for cleft palate in animals is much more difficult than in man. It consists in making an incision on either side, separating the palate from the bone, scarifying the edges and then suturing them together. Harelip in the animal is sometimes readily operable, and is carried out in precisely the same way as in human surgery, by scarifying the edges and uniting them together.

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**The Causes of Incomplete Closure of the Abdominal Wall.**  
**I. Congenital Nonunion of the Abdominal Wall, with Ectopia of Intestine and Bladder, and Rachischisis.**

*Emmy Best, Georg B. Gruber and Theodor Höfling, Virchow's Arch. f. path. Anat., etc., 236:146, Berlin, Jan. 14, 1922.*

Among the abnormalities of ventral union the most frequent cases are those of nonunion of the abdominal wall. This developmental failure is characterized by a marked defectiveness in the structure of the abdominal wall, allowing for an evagination of almost all the viscera, the only covering of the latter, frequently incomplete, being a thin mem-

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brane. There coexist frequently most marked abnormalities in the structure of the vertebral column, and a pelvis without a completely united symphysis pubis.

Marchand describes this type of deformity as follows: "The umbilical opening is so wide that the greater portion of the abdominal cavity remains uncovered. The abdominal parieties, beyond the margins of the opening, are formed by the amniotic sac, which latter envelops the majority of abdominal viscera. The short umbilicus is very often inserted into the lower aspect of the sac—or there may be no umbilical cord, and the sac is directly attached to the placenta."

Another typical feature is the communication with a manifest or occult rachischisis, and a more or less pronounced involvement of the cord. Although these umbilical funicular hernias are among the rarer deformities (older statistics place them as occurring once in 5,000 births), the literature on the subject is quite exhaustive. But since the last word on this highly complex phenomenon has not been spoken, there being a multitude of theories as to the causation of the deformity, the authors contribute a minute description of 3 cases belonging to the eventration group described by Kernauner; since, contrary to the condition in abdominal non-union, there was no free umbilical cord in any of the cases. All 3 cases showed a right convex scoliosis and separation of the symphysis; all lacked the greater distal portion of the colon, including sigmoid, rectum and anus; there was a persistent cloaca (union of lower ileum and bladder); in all cases there were small cutaneous ridges in the groins (persistent genital ridges); there was no division of the genital swelling, but a hypospadias condition of the urethra. There was no anomaly of the diaphragm.

There were some differences of detail in the 3 cases, concerning principally the genito-urinary tract. As far as the teratogenetic termination period is concerned, the authors' findings confirm the investigations of Kernauner. There is also a confirmation of the latter investigator's views as to the formal genesis of the condition described, i. e., that the simultaneous occurrence of abdominal nonunion and curvature of the spine is due to a disturbance occasioned by a primary hydramnios in the metameric body development. It is, however, to be noted that amniotic adhesions may also play a rôle in the production of abdominal herniae.

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**The Theory of Progonoblastomas.**

*Ernst Mathias, Virchow's Arch. f. path. Anat., etc., 236:424, Berlin, Jan. 14, 1922.*

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The work covers tumors arising from germinal outgrowths (not traumatic, nor those appearing postpartum as the result of some pathologic process). The terms progonoma and progonoblastoma refer to revulsions, atavistic reverersions of organ anlagen to ancestral forms. When fetal organs or parts, destined to be only transitory, persist in postuterine life, there occurs an abnormality for which the name atavismus ex persistencia is proposed; thus, for instance, branchial fistulas. These forms of atavism may also be involved in further differentiation, e. g., hypermastia. Then there is a secondary atavism, persistence of embryonic circulatory channels through deviation of the blood stream on account of hypoplasia or agenesis of blood vessels. Primary, or  
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original, atavism is a special form, showing reappearance of organs or rests, ontogenetically discarded, in single individuals, e. g., certain forms of multiple spleens, or annular pancreas. A quite different form from the original is spontaneous atavism, i. e., the reactivation of some function which in the average individual of the species has long become latent. These observations were suggested by studies on tumors of the salivary glands (mixed parotid tumors). Wherever salivary glands exist, phylogenetically, there may occur, by reversion, corresponding tissue rests, which may manifestly quite readily become neoplastic. Perhaps the occurrence of some tumors (endotheliomas) of the tongue, palate and floor of the mouth may be accounted for in some such manner. The same applies to the carcinosomatous tumors (adenomyomas) of the small intestine and their possible origin from scattered pancreatic rests. The conception of carcinoïd tumors of the appendix as choristoblastomas (Gerlach) approaches closely the author's views, since the concept of choristoma partly coincides with that of progonoma. Progonoblastoma is the name given an organoid, neoplastic growth, occurring in a given part of the body by a reversion in the phylogenetic area of development of some organ. Even nevi of the conjunctiva are to be regarded as progonoblastomas. Pigmented nevi of the oral cavity can only be explained through atavism. If in those parts of the body which in animals ancestral to man were generically pigmented there occurs pigmentation, there is potential danger of the occurrence of pigmented nevi and melanomas.

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**A Comparative Study of Normal and Malignant Tissues Grown in Artificial Culture.**

*A. H. Drew, Brit. J. Exper. Path., 3:20, London, Feb., 1922.*

Experiments on rat and mouse tissue and mouse tumors grown on mouse plasma. An embryo heart continued to grow for several days and beat actively; the adult heart gave only a very slight growth in a very small percentage of cases; the growth of the tumors is much less marked than that of the embryo heart. The following solution, the inorganic constituents of which are nearly identical with those of plasma, would give growth but, just as with plasma, growth of the tissues gradually ceased and finally died: NaCl 0.900, KC1 0.042, NaHCO<sub>3</sub> 0.020, CaCL<sub>2</sub> 0.20, CaH<sub>4</sub> (PO<sub>4</sub>)<sub>2</sub> 0.010, MgHPO<sub>4</sub> 0.010, H<sub>2</sub>O 100. The salts must be pure. Drew advises making up stock solutions of the various salts 10 times as strong as the final concentration; 10 c.c. of the NaCl, KC1 and MgHPO<sub>4</sub> solution are then pipetted into a flask and 40 c.c. of distilled H<sub>2</sub>O added. The calcium solution and bicarbonate are steamed in 3 separate flasks, and just before use 10 c.c. of each is pipetted into the mixture. The solution should not be autoclaved, the best results occurring when it is steamed. The finished solution should have a faint bluish opalescence. The pH of the fluid should be 7.4. Growth of tissue was no better when glucose or rat serum was added to this solution. Drew then prepared an embryo extract by finely mincing mouse or rat embryos in a small quantity of the saline solution, freezing and thawing the mass several times for thorough disintegration of the cells, then centrifuging till a clear or faintly opalescent fluid was obtained. Embryonic tissues grew rapidly

and vigorously in cultures containing 2 parts of this extract with 3 of the saline solution. The early death of the cells in the plasma is due to the elaboration of toxic substance which quickly reach alethal concentration. The substance that produced growth in vitro in the experiments with embryonic tissues is found in extracts of these tissues only for it could not be demonstrated in rapidly growing tumors or regenerating tissues of the adult. The degree of difference shown by cultures of normal and malignant tissues is partly conditioned by the accompanying growth of the stroma. The stroma behave in culture like embryonic tissue rather than like the adult tissue from which it is derived.

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**The Carbohydrate Metabolism of Surviving Mouse Tissues and Tumors.**

*B. R. G. Russell, Brit. J. Exper. Path., 3:51, London, Feb., 1922.*

Present research is a continuation of a paper published on the respiratory quotient of surviving tissues of the mouse. The procedure consists, briefly, in the measurement of the changes of volume observed in an air space containing a known amount of finely-divided tissue or tumor suitably disposed to facilitate the respiration of the cells. In this research a modification of the well-known Barcroft blood-gas analyzer was used. Russell purposed to find out whether a low respiratory quotient indicated that a tumor strain could consume carbohydrate only to a limited extent, or whether it only meant that in the parenchyma there was no readily available supply. All the sugars tested, including glucose, levulose, galactose, maltose, saccharose and lactose, were made up into a 2:1000 solution. As a diluent, an 0.85% saline solution made with tap water was used. The respiratory quotients for mouse kidney and heart, a sarcoma of very rapid growth, 2 carcinoma strains of slow growth, and a sarcoma of rapid growth, are shown in tables. Glucose and maltose seem to be attacked by all tissues with equal facility, while galactose and saccharose are neglected. The burning of levulose by kidney and one sarcoma is missed in another, and only faintly indicated by the 2 adenocarcinomas. Kidney substance consumes lactose.

The addition of glucose to emulsions of the 4 different tumor strains raised the respiratory quotient to about unity in all cases. The rise is particularly striking in 2 strains which ordinarily have low quotients of from 0.7 to 0.8. These experiments demonstrate that the cells of these slowly growing tumors are quite capable of dealing with an adequate supply of glucose, and that there is not an anatomic difference between their blood supply and that of the more rapidly growing tissues. After consideration of the results of these experiments, Russell concludes that the cells of slowly growing tumors have a lesser amount of carbohydrate in a readily available form.

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**The Infectious Tumor of Birds. Its Significance in the Experimental Study of Neoplasms.**

*Albert Peyron, Paris méd., 12:146, Feb. 18, 1922.*

Peyron mentions the experiments of Rous on the infectious sarcomas of chickens which for the first time showed the existence of a (Sec. 1—Page 783)

specific virus distinct from neoplastic cells, and possessing the property of reproducing the same. It is emphasized in the first place that contrary to the assertion of some authors, the infectious tumor in question is a real neoplasm and not a simple inflammatory lesion. By following its development day by day, the author saw that between the second and third week it had absolutely the same structure and vascular organization as the most typical human sarcoma, although later on secondary necrotic processes took place in the central part of the tumor. When the pectoral muscle of an animal is injected with this virus a process of regressive differentiation may be observed. At first the muscle cells proliferate, giving rise to muscular fibers, but the growth gradually takes on the characters of a myosarcoma and finally becomes identical to a sarcoma originating from the proliferation of the interstitial connective tissue. Peyron has been able to obtain metastases of these tumors which showed an almost pure type of rhabdomyoma. When a filtrate of the tumor is injected into the peritoneal cavity a vegetating neoplasm is produced which originates principally from the proliferation of the endothelium with the accessory participation of new growths of underlying elements. There are also two varieties of infectious tumors produced by a filtrate free from cellular elements which assume the type of an osteochondro-sarcoma. The tumor first goes through a stage analogous to sarcoma and then forms cartilage and osseous tissue. Metastases of this tumor are found in most of the viscera, so that in every respect it is similar to an ordinary neoplasm. These experimental tumors can be obtained both with filtrates of a tumor or with the blood serum. It is not settled yet whether one or several kinds of virus correspond to the various types of tumors, but in view of the above facts Peyron is inclined to consider that this virus may be polyvalent.

From a histogenetic point of view there is no doubt that the infectious tumors of birds can be assimilated to the neoplasms of mammals and man. There seem to be on the other hand wide differences as regards their progress, since these tumors become generalized in four to six weeks in chickens. Such differences may be explained partly by the special physiological conditions of these animals and also by the fact that experimentation gives an added impetus to the growth of the tumors. It is interesting to note from an etiological point of view that traumatism plays a definite rôle in infectious sarcoma as in the human variety, although certain pathologists have taken this fact as an argument against the infectious nature of sarcomas. On the whole it may be concluded that the infectious tumor of birds is not so different from human tumors as appears at first sight, and although Peyron does not believe that all neoplasms have an exclusively infectious origin, this seems more and more likely as regards sarcomas.

From an experimental point of view it has been shown that ultra-violet rays or radium do not destroy the virus in a graft, although the cells themselves may be killed out. A tumor filtrate which is exposed for twenty-four hours or longer to the action of radium remains also pathogenic. Peyron so far has been unable to determine the optimum dose to be applied to cause the disappearance of the cellular growth. Sometimes a permanent sterilization of the tumor is produced while in other cases its growth and metastatic dissemination are greatly stimulated.

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**Silicon, Calcium and Magnesium in Carcinomatous Tissues.**  
*Albert Robin, Bull. Acad. de méd., 87:128, Paris, Jan. 31, 1922.*

Robin's previous researches have shown that carcinomatous tissues absorb an excess of certain mineral substances, while they become demineralized as regards others. He classed these substances into 2 groups, one that seems to be concerned with the building up of the neoplasm (chlorin, sodium, potassium) and the other which is looked upon as representing defensive agents (silicon, magnesium, calcium, phosphorus, iron).

Silicon, magnesium and calcium were administered to 3 patients suffering from carcinomas of the colon, esophagus and liver in order to ascertain whether these minerals would be fixed by the cancerous tissue. The organs were analyzed after death and compared to a healthy liver and also to 2 cancerous livers of untreated patients. This investigation showed that all 3 elements and especially silicon were fixed by cancerous tissues. It is known that silicon is the essential mineral constituent of connective tissue, the rigidity of which is proportional to the quantity of this element contained by it. It was observed in this connection that the fibrous texture of these tumors was strongly developed. The administration of silicon appears, therefore, to be indicated in order to supply the substance necessary for one of the spontaneous defensive processes of the organism against cancer. It is not known by what process magnesium and calcium contribute to this defense. We only know that in cancers undergoing regression the calcium contents increase markedly, and that in slowly progressive carcinomas of the liver, magnesium accumulates in the uninvaded regions, which justifies the hypothesis that these regions owe their resistance to the accumulation of magnesium.

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**Neuroblastoma Sympathicum.**

*Barnewitz, Frankfurt, Ztschr. f. Path., 26:317, no. 2, Wiesbaden, 1921.*

Herxheimer, basing his discussion on 1 case which came under his own observation, proposed to describe the tumors consisting of immature elements of the sympathetic as neuroblastoma sympathicum. Up to the present, only a few cases of this kind have been observed and described with sufficient details. Barnewitz describes 1 case belonging to this category, which is of a special character owing to the localization of the multiple tumors and the histological aspect. In a woman of 37, a tumor the size of an apple was found in the superior lobe of the left lung, another tumor of the same size in the place of the right suprarenal capsule, and 2 tumors, exceeding a large man's fist in size, in the place of the 2 ovaries. Histologic examination showed that the tumors consisted of immature elements of the sympathetic nervous system and must therefore be described as neuroblastoma sympathicum. The suprarenal tumor represented the primary tumor; the ovarian and pulmonary tumors were evidently metastases. The cells of the tumor were sympathoblasts which do not differentiate into sympathetic ganglion cells, but reach only intermediate stages; the interstitial substance, composed of fine fibrils, is neither neuroglial or nervous tissue.

but fibrin. Nerve fibers could not be demonstrated. The patient's advanced age was another discriminating feature. If the congenital nature of this tumor is to be insisted on, it must be assumed that its power of proliferation was dormant for a long time and was then suddenly excited by some unknown cause. But the fact remains that in this particular case, in contradistinction to all previous observations, neuroblastoma sympatheticum was established in a full grown person.

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**Cartilaginous Exostosis of the Parietal Bone.**

*Edward Hübscher, Frankfurt. Ztschr. f. Path., 26:332, no. 2, Wiesbaden, 1921.*

Exostoses of the cranial vault are among the more frequent secondary findings at autopsy. According to their structure, they are divided into exostosis eburnea, spongiosa and medullaris; genetically, they belong to exostosis fibrosa, since they originate in that portion of the skull which is performed as connective tissue.

The case described by Hübscher differs at once from the ordinary exostoses of the cranial vault in that it is a case of exostosis cartilaginea. It was revealed by autopsy on the body of a girl of 22, who had died of tuberculous meningitis. The tumor, situated on the inner surface of the left parietal bone, was of a polypous aspect and measuring 25 by 20 by 13 mm.; the surface was extremely nodose. The individual nodules were partly roundish and partly of an irregular configuration, with a diameter of 3 to 10 mm. The nodules were separated from each other partly by shallow and partly by deep grooves, so that the surface of the tumor was very irregular. The consistence corresponded in most places to that of cartilaginous tissue; only at the pedicle, which was sawn through, a somewhat irregularly shaped tongue of cartilage. The pedicle just mentioned was conspicuous on a section right through the tumor; it was surrounded on the outside by cartilaginous tissue in a width of 3 to 10 mm., so that the tumor might be described as passing into the parietal bone (which has unfortunately not been preserved) by means of pedicle, consisting of cartilaginous and bony tissue, and measuring about 1 cm. in width. By far the largest part of the tumor was occupied on the surface of the section by typical cartilaginous tissue of a breadth of 3 to 4 mm. on the average, and surrounding a transverse cyst, measuring 16 by 6 mm., with the individual cartilaginous lobes and also the bony tissue protruding somewhat towards it. In the postmortem report, it was described as a typical cyst formed by the softening of the tissue, and as containing cartilaginous tissue affected by myxomatous and edematous degeneration. The first examination had already revealed typical hyaline cartilage with medium-sized cartilage cells in teased preparations and spongy bony tissue in the pedicle. Hübscher subjected the material to an additional microscopical examination after embedding it in celloidin. The cartilaginous portions, which still yielded comparatively good results in regard to nuclear staining, notwithstanding their age, consisted of a hyaline homogeneous cartilaginous matrix with a medium number of cartilage cells, partly polyhedral and partly more or less irregular. The lobate structure of the tumor, limited on the outside by

tions. The bone portions consisted of rather thick spongy bones with distinct bone corpuscles and trabeculas of a fine lamellar structure. Some fat-marrow was present between the latter; osteoblasts and osteoclasts were scarce. The transition between cartilage and bone showed partly direct metaplasia of cartilaginous and bony tissue, and partly calcification of the cartilaginous matrix, accompanied by an increase of the cartilage cells and by proliferations in the bone-marrow spaces, and formation of bones on the calcified cartilaginous matrix by osteoblasts. Macroscopical and microscopical examination made it absolutely plain that this was a case of exostosis cartilaginea, still consisting, for the greater part, of hyaline cartilaginous tissue. The exostosis encroached broadly upon the paries through bony and cartilaginous tissue. Whether the tumor originated in the paries itself or in the inner periosteum, i. e., the dura mater cerebri, is a question which it is difficult to decide on the basis of the prepared material. But the defect of the dura mater in the region of the tumor, mentioned in the postmortem report, rather pointed to a periostal origin of the exostosis.

Such conditions are found only in very rare cases. The derivation of the cartilage presents difficulties. One has to consider a development on phylogenetic grounds and from bones preformed as connective tissue, for reasons analogous to those for which, in fractures of bones preformed as connective tissue, cartilage is first formed in the callus.

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**Lipoma-Like Hamartoma of the Lung.**

*Adolf Feller, Virchow's Arch. f. path. Anat., etc., 236:470, Berlin, Jan. 14, 1922.*

In a woman who had died at the age of 66 from senile debility there was found in the middle lobe of the right lung a tumor measuring 9 by 11 cm., looking histologically like a mass of adipose tissue; it had developed within the wall of a bronchus, had grown into the lumen of the latter, was traversed by partly normal, partly misshaped, bronchial ramifications, and contained cartilage, connective tissue, bronchial and alveolar epithelium. The mass was therefore not strictly speaking a neoplasm, but a hamartoma (Albrecht), more specifically a hamartoma originating peribronchially, situated intrabronchially, and prevailingly lipomatous structurally. The well-known chondromas of the lung are also said to be classifiable among the hamartomas.

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**Classification of Neoplasms.**

*Browicz, Polska gaz. lek., 1:1, Warsaw, Jan. 1, 1922.*

Certain writers of the Institute for Pathologic Anatomy in the University of Warsaw classify neoplasms according to their starting point, the participation of blastodermic vesicles according to Hornow-skis classification. Browicz is not in favor of eliminating names which indicate simultaneously the manner of formation and the composition of the new-growths, and he particularly opposes the elimination of "carcinoma" and "sarcoma." It is only necessary to indicate precisely what is to be understood by this nomenclature. If we do not consider carcinoma as an atypical epithelial neoplasm, but as a tissue which, in its

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histologic structure, differs from normal epithelial tissue by the arrangement of the cells and by the inter-relation existing between cellular accumulations and blood-vessels and connective tissues, and if we describe it as a medullary, scirrhou, melanotic carcinoma with cylindroform cells, it is quite clear what kind of tissue is meant, as far as its structure and its importance for the organism are concerned.

The choice of the term is not unimportant, for it should not only define the nature of the disease, but should also be easily comprehensible for purposes of diagnosis, prognosis and therapy. An originally local neoplasm, although not unimportant, on account of its size, its location and its possible influence upon the adjoining tissues, may subsequently injure the organism very severely. A fibroma of the uterus (a term which indicates only the kind of tissue and the origin of the cells) may be affected by degenerative changes. The cells of the connective tissues may begin to grow abnormally, assume early forms, become "anaplastic." The neoplasm loses its fundamental character, since the original tissue disappears and is sometimes replaced by profusely vascularized cellular tissue. This transformation may then be called sarcomatous fibromyoma.

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**Cell Infiltration into Dead Corneas.**

*Hans Otto Neumann, Virchow's Arch. f. path. Anat., etc., 236:45, Berlin, Jan. 14, 1922.*

To disprove Grawitz's teaching about the "awakening of the slumbering cell," new experiments were undertaken on fresh and variously heated corneas, injected subcutaneously and intraperitoneally into guinea-pigs. The widely varied tests showed that at given temperatures cell infiltration in Grawitz's sense is actually absent; thus, for instance, it occurs at 56° C., but not at 63°. In explanation of his findings, however, Neumann arrives at diametrically contrary conclusions. An elevation of the temperature to which the corneas were previously subjected causes a gradual reduction and final disappearance of their intercellular spaces and fissures. The mechanical impermeability of the cornea thus obtained results in an absence of cell infiltration. A longer period of implantation would then be required during which the defence cells could work their way into the dead tissue. Cells from surrounding structures wander into these killed corneas. Grawitz's error consisted in his failure, during his experiments with heated corneas, to take into account the physical changes occurring in the latter.

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**Postmortem Acid Formation and Rigor in the Heart Muscle of Human Cadavers, and Their Relation to the Energy Capacity of the Heart. Immediately Preceding Death.**

*J. Oberzimmer and L. Wacher, Virchow's Arch. f. path. Anat., etc., 236:225, Berlin, Jan. 14, 1922.*

The muscle extracts of some cadavers show very little or no postmortem acid formation, while there is much potassium albuminate present; such dead muscle acts exactly like living tissue. It was shown that low acid formation in such cases coexisted with light rigor mortis.

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In the cases which gave no postmortem acid formation, no glycogen could be found in the muscle. The present work had for its object to investigate whether there was any parallelism in the lack of postmortem acid formation between skeletal and cardiac muscle. The investigations showed that the postmortem acid production sets in sooner in the cardiac than in skeletal muscle, attaining its peak in two hours. The acid-alkali ratio is almost always greater in the left ventricle than in the right or in any skeletal muscle; deviations from this rule always occur with cardiac affections. In cases of disease associated with cachexia (tuberculosis and cancer) very little acid is formed in the cardiac or skeletal musculature, most of it being found in the left ventricle. From estimations of the postmortem acid formation, with values for the acid-alkali ratio below 1, one can diagnose with certainty an insufficiency of the ventricle under investigation. This chemical examination is of no avail in cases of death from cerebral disturbances or sudden circulatory obstructions. In greatly hypertrophied ventricles the postmortem acid formation is very high. Brown atrophy of the heart muscle did not affect the extent of postmortem acid production.

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**Fatty Infiltration of Voluntary Muscle.**

*Kolodny, Virchow's Arch. f. path. Anat., etc., 236:270, Berlin, Jan. 14, 1922.*

Muscles of the diaphragm, pelvis and tongue of 250 cases taken at random were investigated. It was shown that fatty infiltration into voluntary muscles is not found regularly, and is not to be regarded as normal. The fat content is proportional with the capability of the muscle for work, being almost totally absent in the muscles of the newborn and increasing progressively with advancing age. Diseases causing disturbances in circulation are frequently accompanied by fatty infiltration of muscles. The condition bears no relation to diet; it represents a macroscopic, easily detectable sign of muscle degeneration. No conclusions as to the condition of the muscle cell can be drawn from the form of its fat content (small fat droplets or large fat globules). Lubarch adds a note, stating that he admits that the presence of fat in voluntary muscles is not physiological, that the various muscle groups and single fibers are unevenly affected, and that the most active muscles are the seat of the most extensive fat deposits. But he thinks it has not yet been demonstrated that fat infiltration represents a state of degeneration.

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**On the Origin of the Free Cells of Serous Exudates.**

*R. S. Cunningham, Am. J. Physiol., 59:1, Feb. 1, 1922.*

Two general methods were used for the experiments upon which this report is based. Animals (cats and rabbits) were stained by the intravenous administration of vital dyes, an irritation of one or more serous cavities induced, and the exudative and tissue-cells studied in living and fixed preparations. In other animals the staining and irritation were accomplished by introducing the solution of the dye directly into the serous cavity, thus giving the cells of the exudate and those lining the cavity every opportunity to ingest the dye. In all cases

the cells of the exudate, the omentum, and cells scraped from the serous surfaces were studied living, both with and without supravital staining. The majority of the experiments were carried out on the peritoneum but all crucial ones were repeated on the pleura, some of the experiments upon both pleural and peritoneal cavities were carried out on the same animal. The dyes used for vital staining were Grubler's trypan blue, Niagara blue 3B, and crude Niagara blue.

In discussing to what extent the lining cells of the serous cavities participate in the formation of the cells of the exudates following any type of stimulation in these areas, the authors remark that certain definite views have become formulated, namely: (1) that serosal cells desquamate as typical flat cells and then act as primitive stem-cells capable of undergoing differentiations through several stages to become monocytes or special granular leucocytes; (2) that these cells swell as the result of irritation, become changed in shape, put out processes, detach themselves from the basement membrane and continue life as free, living, typical, highly specialized macrophages; (3) that serosal cells are incapable of becoming free, living exudate-cells but can, during inflammatory reactions, act as vasoformative cells or can change to fibroblasts; (4) that they are highly specific lining cells capable of no further differentiation, and that any of them desquamating are injured or degenerated after becoming free; and that the changes taking place in them during an irritation represent some exaggeration or modification of normal functions and attributes. The theory that the flat, normal, serosal lining cells desquamate immediately upon being irritated and later, while free in the cavity, undergo differentiation into characteristic exudate-cells, is based wholly upon morphologic data.

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**Cloudy Swelling a Process of Stimulation.**

*Anna Davidman and David H. Dolley, J. M. Res., 42:515, Oct.-Dec., 1921.*

Davidman and Dolley observed the effects on the livers of frogs and of white rats of thermal, trophic, and normal and abnormal chemical stimuli, the majority of which are known to produce cloudy swelling. The one common effect was some phase of stimulation, either an excitation, or a depression, or a combined process of primary excitation, followed by secondary depression, the particular reaction depending upon the intensity and duration of each sort of stimulus. The morphologic effects are identical with those in the nerve cell after the same diversity of stimuli. The phenomena of stimulation thus produced are identical with those classed as cloudy swelling and hydropic or vacuolar degeneration, and the latter can be interpreted in terms of stimulation and cell irritability. The typical alterations of associated swelling and granularity are the result of the most common manifestation of abnormal stimulation, namely, an initial excitation followed by secondary depression. The determination of the effect depends entirely on the intensity and duration of the stimulus. The same stimulus which with slight intensity or short duration produces excitation, with increased intensity or long duration produces depression. The fact that function itself is a process of excitation is cited to explain the similarity between the changes of function and those of cloudy swelling. There

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is no specificity in the primary reactions of stimuli. Abnormal stimuli produce the same effects within the same quantitative range as are produced by natural stimuli.

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**Experimental Pigment Cirrhosis Due to Copper and Its Relation to Hemochromatosis.**

*F. B. Mallory, Frederic Parker, Jr. and Robert N. Nye, J. M. Res., 42:461, Oct.-Dec., 1921.*

Hemochromatosis is defined as a chronic disease due to a definite toxic agent which unites with the hemoglobin set free by the normal disintegration of red blood-corpuscles. Hemofuscin is deposited, as a result, in various cells throughout the body; first and in largest quantities in the liver; later in the pancreas, heart, kidneys, adrenal glands, and other organs and tissues. Usually, but not always, the hemofuscin is transformed into hemosiderin.

The deposit of pigment in parenchymatous cells (liver, pancreas, heart) causes necrosis of some, followed by active regeneration of others. The pigment set free by necrosis is taken up in large quantities by endothelial leukocytes. The connective tissue in some organs is gradually increased owing to new formation of fibroblasts, as in tumors, which form stroma for the islands of regenerated cells. The sclerosis is due to contraction and coalescence of old stroma as the pigmented cells die off.

The final result of these processes is cirrhosis of the liver, sclerosis of the pancreas with consequent diabetes mellitus, sclerosis of the heart. The pigmentation of the skin may be due in part to injury to the adrenal glands.

It is concluded from experimental observations that it is impossible in a few months to produce lesions for which nature requires years. Chronic poisoning with salts of copper produces in the livers of rabbits in six months to a year a series of changes comparable to those found in the human liver in hemochromatosis. Poisoning with smaller doses continued over a much longer time would probably cause lesions in other organs. If hemochromatosis is due to poisoning with copper there are several sources from which it may be derived: (1) From its use as a coloring reagent to copper vegetables (pickles, canned peas and beans) and to improve the color of absinthe. (2) From its use as an anti-septic to prevent fermentation (beer, wine) or to inhibit the growth of algae (drinking water). (3) From distilled liquors (action of acids, chiefly acetic, on copper and brass tubing used in connection with stills).

(1f-89)

**Fatty Changes in the Liver, Heart and Kidney.**

*C. G. Imrie, J. Path. & Bacteriol., 25:26, Edinburgh, Jan., 1922.*

In a previous paper Imrie attempted to determine whether the law that was found to hold for fatty livers, held also for fatty hearts and kidneys. Indications showed a relationship of this kind. In the present paper 2 series of observations have been made the results of which throw some additional light on the significance of fat in these organs. The first of these deals with the distribution of fat in the heart

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in certain special cases. The hearts of 2 cases of pernicious anemia showed in the subendocardial samples taken from the cases a higher degree of fatty change than has ever been found before—4.5 and 5.3% additional fat, respectively, as compared with more externally placed muscle.

The other series of observations were made on the fatty changes in the organs of 9 dogs by the subcutaneous injection of .5 to 1.5 c.c. of pulegone given daily for five or six days. The average fat value for the heart in the experimental animals was 3.41% with an iodin value of 1.31. For the liver the average fat value was 9.27% with an iodin value of 96.5. Control dogs were used. The writer states that these results show clearly that if there is no qualitative difference between the liver and the heart, the quantitative difference is so great that it is necessary to give, as Leathes has pointed out, a physiological significance to the variation in the liver which is unnecessary in the heart.

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**The Effect of Stored Glycogen upon the Autolysis of Liver Tissue.**

*J. P. Simonds, F. H. Reuling and H. H. Hart, J. M. Res., 42:455, Oct.-Dec., 1921.*

Continuing their previous studies on the effect of glycogen on the autolysis of liver tissue, Simonds, Reuling and Hart carried out experiments with livers whose content of glycogen had been increased by a carbohydrate diet. The observations were made on dogs. The animals in one group were fed large amounts of sugar so that the glycogen content of the livers was abnormally high; those in another group were treated with subcutaneous injections of phlorizin so as to render the liver practically glycogen-free. It was found that the autolysis, *in vitro*, of the livers of the phlorizinated dogs was always more rapid and in greater degree than that of the livers of the sugar-fed animals. Autolysis of the livers in dogs on the usual diet was slightly more rapid and complete than of those in the sugar-fed dogs, but considerably less than in the animals injected with phlorizin.

Microscopically, the phlorizin livers were found to contain much fat but no demonstrable glycogen, while the cells of the sugar-fed livers were packed with granules of the substance. The livers of normal dogs showed somewhat varying amounts of glycogen, always more than the livers of the dogs treated with phlorizin and less than those of the dogs fed on sugar.

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**Pathologic Anatomy of the Spleen.**

*Kubik, Frankfurt. Ztschr. f. Path., 26:285, no. 2, Wiesbaden, 1921.*

In consequence of the tendency of carcinoma to spread through the lymph circulation, and in accordance with the significance of the spleen as a gland intercalated in the vascular system, carcinomatous metastases in the spleen are observed only in comparatively rare cases. In general, this can occur only if the tumor has penetrated a blood-vessel.

Kubik gives a description of one case, which tends to show that the macroscopic aspect frequently suggests the diagnosis of carcinomatous metastasis, when, as a matter of fact, it is not present, and that, even in peritoneal carcinosis and after irruption of the carcinoma into the vascular system, it is well to proceed with great reserve. In a woman of 39 years, carcinoma of the stomach was found together with nodules of the spleen, which were interpreted as metastases. Microscopical examination, however, showed that the nodules consisted of fibrous tissue; in two places, remainders of follicles were found. This is, therefore, not a case of carcinomatous metastasis, but of *induration circumscripta*, as described by Poscharissky—an affection which is not congenital, but acquired, as appears from the slow progress.

In another case, autopsy on a tuberculous patient revealed a blood cyst, of the size of a fist, in the spleen beside the hilum. The contents consisted of a splenic tissue and blood, but they were not yet demarcated. There was no indication of a trauma; tuberculosis might be considered as an etiologic factor; tubercular nodules were present in all the layers of the spleen.

In still another case, a node of the size of a cherry was found in a spleen otherwise normal. Histologic examination showed that the tumor was without capsule and consisted of follicle and pulp like a normal spleen; it contained an abundance of pigment. This node must be interpreted as an accessory spleen within the spleen; it showed transformations (cyanotic induration) which were not present in the primary organ.

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#### An Anatomic and Pathologic Study of the Thymus in Infants.

*Adolfo F. Canelli, Pediatra, 30:58, Naples, Jan. 15, 1922.*

Canelli has studied the system of reticulate fibers in the thymus in 104 subjects, among whom many were affected by hereditary taints, or with atrophy or marasmus as a result of chronic illness. He maintains that under normal conditions the thymus has no reticulate fibers in the first 5 months of intra-uterine life. Later the fibers are quite scarce in the cortical substance, less so in the medulla, and well distributed about the vessels. About the lobules they form a thin reticulum, which, seen in section, assumes the appearance of a basal membrane. In the new-born and in subjects up to 3 years of age, the fibrils are less scarce, the perilobular reticulum is more evident, and several fibers branch out from it and from the perivascular sheath towards the internal parenchyma, where they are distributed irregularly, often terminating at the walls of a vessel. Between the ages of 4 or 5 and 15 months, the reticulate fibers are numerous and constitute a more or less wide-meshed reticulum which crosses an entire lobule, either in the peripheral or central stratum. The cellular elements are found within the meshes, more numerous in the peripheral than in the central zone. They do not constitute a sharp division between the cortex and the medulla of the organ. The reticulate fibers are seen neither about nor within Hassals corpuscles. After 15 months the reticulate fibers predominate in the thymus; they are distributed less irregularly in the

two substances than they were in the previous period, are numerous about the vessels, and are found about Hassal's corpuscles.

In the incipient adipose transformation of the thymus, when the distinction between the cortical and medullary substances is less evident, and the little round cells and the epithelial cells are irregularly distributed in the lobule, the reticulate fibers are abundant in the adipose tissue.

In the thymus of hereditary syphilitics, and in the thymus affected by sclerosis, the system of reticulate fibers is generally well developed in the fetal state, in infancy, and in childhood. It is sometimes so greatly developed that the entire lobule is invaded by it, with complete loss of differentiation between cortex and medulla and with irregular arrangement of the small round cells and the epithelial cells.

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**Pathogenesis of Morbus Addisonii.**

*A. Bannwart, Frankfurt, Ztschr. f. Path., 26:307, no. 2, Wiesbaden, 1921.*

Bannwart describes a case which, contrary to other recent observations, shows the significance of the medullary substance of the suprarenal capsules and of the chromaffin system in regard to the pathogenesis of Addison's disease. The patient in question, a man of 45, exhibited the symptoms of this disease in a pronounced manner. Autopsy revealed a malignant tumor, which was interpreted as typic lymphangioendothelioma of the peritoneum. It had led to numerous metastases in almost all the organs of the body, including the 2 suprarenal capsules. The medullary substance of the latter had been entirely replaced by the tumor, whereas the cortex remained intact to a considerable extent. The funiculus marginalis was largely permeated by tumor. This case, accordingly, tends to prove that, at the beginning of Addison's disease, an isolated affection of the medullary substance of the suprarenal capsules may be present. In consequence of the complication by carcinoma, the patient died at a time, when the cortical transformations had not yet reached development, which is not usual in ordinary cases of Addison's disease.

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**Studies on the Pneumonic Exudate. V. The Relation of Pneumonic Lung Protease Activity to Hydrogen-Ion Concentration, and a Consideration of the Origin of the Enzyme.**

*Robert H. Nye, J. Exper. Med., 35:153, Feb., 1922.*

Washed cellular suspensions of pneumonic lungs contain a protease or proteolytic ferment, derived chiefly from the leukocytes of the exudate. It is most active in a slightly alkaline medium. The enzyme seems to be the one causing the digestion of the fibrin. In preparation of the extract from pneumonic lung, the organ is ground in a meat chopper, washed in gauze and centrifugalized to yield a cellular suspension. Digested proteins are determined by the Kjeldahl method and van Slykes method for the amino-nitrogen.

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**The Large Exudation Cells in Tuberculous Meningitis and Caseous Pneumonia.**

*Ferdinand Wiedhold, Frankfurt. Ztschr. f. Path., 26:341, No. 2, Wiesbaden, 1921.*

Tuberculous meningitis is one of the forms of tuberculous inflammation in which exudation is more pronounced than proliferation. As a rule, tubercles of a really typical nature are not developed. Giant-cells are not very frequent. Nevertheless, the aspect of tuberculous meningitis is sufficiently characteristic on account of the nodular, perivascular exudation and, above all, on account of the kinds of cells involved. The latter do not consist of the ordinary pus corpuscles, the polymorphonuclear leukocytes, which are found only as isolated specimens, but almost entirely in small round cells and peculiar large varieties of cells. These large cellular elements are not found exclusively in meningitis tuberculosa, but also in other inflammations of the leptomeningix, acute as well as chronic. But it is in a certain sense typical of tuberculous meningitis that they form a considerable proportion of the exudation cells—sometimes as much as half of them or more.

Wiehold subjected these peculiar cells to a careful examination, in 14 cases of tuberculous meningitis and 9 cases of caseous pneumonia. The specimens were taken as soon as possible after death, from those portions of the cerebral surface which were typically diseased and sometimes also from those which were only slightly affected; they were then fixed in formalin, formal-Müller fluid, alcohol, Zenker's solution, and Zenker-Helly's fluid, and embedded in paraffin or, in some few cases, in celloidin. The staining methods employed were the hematoxilineosin method, van Gieson's method, Weigert's method for fibrin, and toluidin-blue, the latter 2 producing the most satisfactory results in regard to nuclear staining. For the demonstration of possible granula, the usual blood stains were employed (Giems'a method, May-Grünwald solution, Ehrlich's triacid) and further the methyl-green-pyronin stain, Ellermann's granula stain, the oxydase reaction, and Altmann-Schridde's method. In tuberculous meningitis, the cells proved to be macrophages, which do not produce oxydase reaction. In caseous pneumonia, the cells are mostly desquamated alveolar epithelia, while the lung stroma is frequently infiltrated with round and plasma cells. In both cases, therefore, the exudation cells are descendants of fixed tissue cells—in the one case epithelial, and in the other connective tissue and endothelial cells—histiocytes on which some special function was probably incumbent in the fight against the tuberculous virus, which finds its morphologic expression in a characteristic change of form, separation from the cellular organization and phagocytosis.

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**Bacteriologic and Historic Examinations of the Fat Marrow of the Femur in Typhoid Fever.**

*Adolf Hartwich, Frankfurt. Ztschr. f. Path., 26:227, no. 2, Wiesbaden, 1921.*

Following up Eugen Fraenkel's investigations, author undertook systematic examinations of the marrow of the femur in typhoid fever. His material comprises 12 cases referring to patients from 6 to 51  
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years of age; 1 died at the beginning of the second week, 3 within the second week, 2 during the third week, 1 in the fourth week, and the others during the fifth, sixth and tenth weeks respectively. In all these cases, Hartwich succeeded in cultivating typhoid bacilli from the marrow of the femur and the vertebrae on Drigalski-plates, whereas culture in blood, spleen and gall had negative results in several cases. The number of bacilli was independent of the stage of the disease; they were also found in pure fat-marrow. The numbers of the colonies derived from the femoral marrow were, as a rule, inferior to those derived from the vertebral marrow; but there was no regularity in that respect. In some cases, mixed infections were present, other germs such as pneumococci and streptococci being cultivated from the marrow, in addition to the typhoid bacilli. Macroscopically, the marrow presented the same aspect as in other infectious diseases; in younger patients, it was more red marrow; in older persons, it was in part red and in part fat marrow; there were no circumscribed transformations. But histologically, it was always possible to establish minute necrotic areas, in some cases with and in others without formation of fibrin, in the place of which an indifferent tissue develops in the course of regression, which is analogous to a cicatrix. Generally speaking, the areas without fibrin are more frequent than those containing it. The histological examination further showed that the necroses are apparently not caused by the bacteria but by their toxins. Hartwich was also able to establish that, in typhoid, there is nearly always an increase of lymphocytes in the bone-marrow; in three cases (concerning children) lymph-follicles were found in the marrow. With respect to the increase of lymphocytes in the femoral marrow in cases of typhoid, Hartwich refers to analogous investigations by Schur and Loewy (*Ztschr. f. klin. Med.*, 1900, 40), who discuss the question as to whether, in the individual cases, the transformation of the marrow in the tubular bones is of a more lymphocytic or myelocytic character, according as the lymphocytes or the granular mononuclear cells, the myelocytes, are in the majority. Of 4 cases of typhoid, 2 exhibited lymphocytic marrow, 1 myelocytic and 1 hyperemic fat-marrow. It is not inconceivable that the more frequent occurrence of single lymphocytes, embedded between the other cells of the femoral marrow, might be connected with the affection of the lymphatic apparatus in typhoid.

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Section of Tropical Medicine, Army Medical Museum, Washington, D. C.

G. R. Callender, *Am. J. Trop. Med.*, 2:67, Jan., 1922.

In spite of the fact that many of the colonies of the United States are either tropical or subtropical, pathological specimens illustrating the so-called tropical diseases are relative rarities in the museums of this country. The Army Medical Museum collections illustrating those diseases commonly considered tropical, and including particularly insect-borne diseases and those due to animal parasites, are being grouped together as covering most of the diseases of special interest to students of tropical medicine. This museum desires to so combine its activities with other museums and pathological departments that a general exchange system may be inaugurated of benefit to all con-

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cerned. At the same time it will maintain in its own collections adequate material for the study of any group of diseases, no matter how unusual they may be. For forwarding specimens to the museum either follow out the Kaiserling process or harden in 10% formalin from one to three days. Adequate histories and recorded physical examinations should accompany the specimen. The specimens are prepared, photographed and mounted on receipt. The descriptions, clinical notes and histological slides are filed. Copies of these are sent to those furnishing specimens. The museum is always glad to receive pathological specimens of all varieties.

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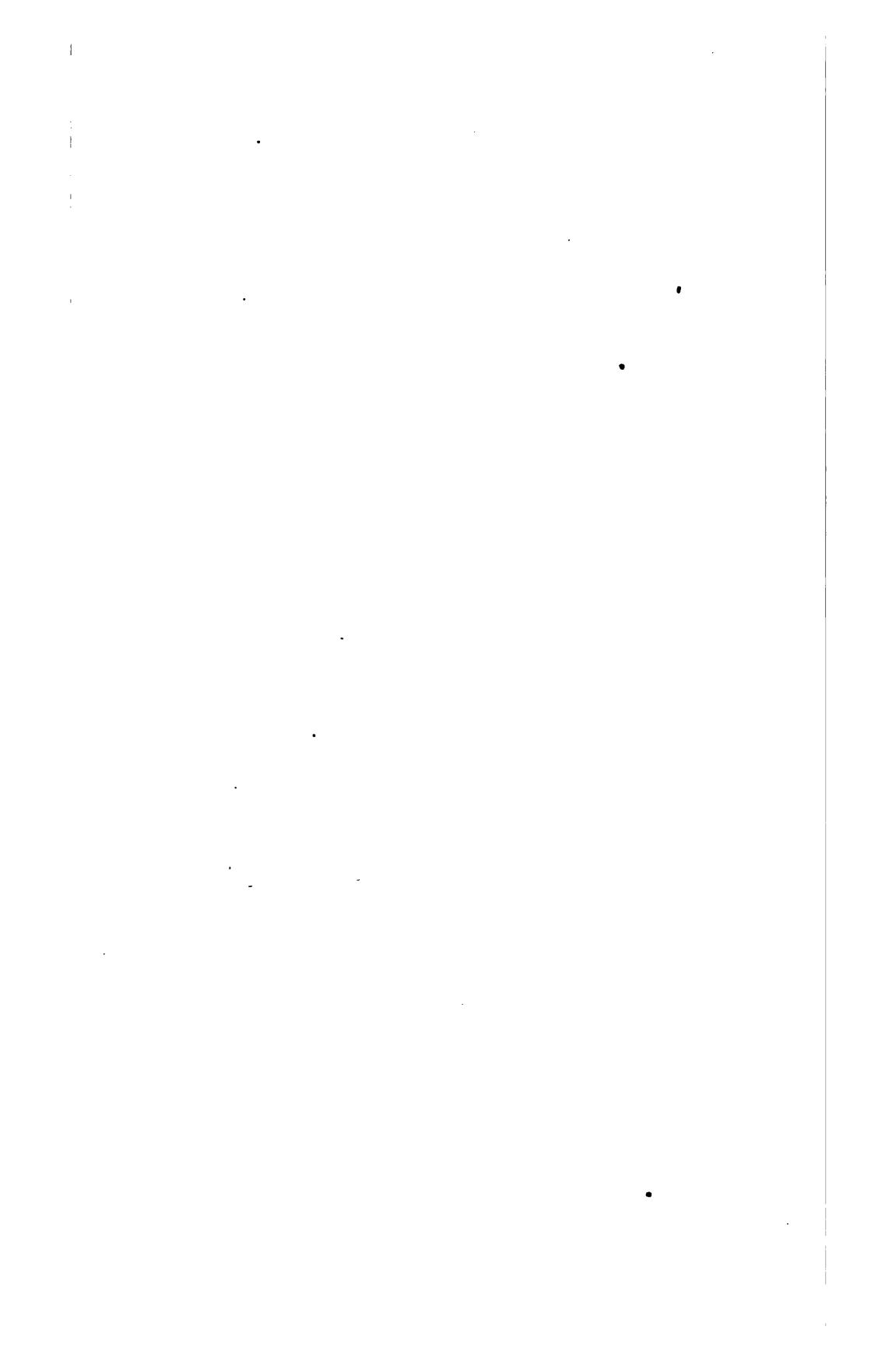
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**The Study of the Pathology of Hamsters.**

*Hugo Reinhardt, Virchow's Arch. f. path. Anat., etc., 236:1, Berlin, Jan. 14, 1922.*

The author took advantage of the fact that hamsters are kept in the St. George Pathologic Institute at Leipsic for special serologic research work, and studied about 120 animals in order to ascertain the pathology of the species. No structural abnormalities were found; one specimen revealed a spindle-cell sarcoma of the mandible. A special disease found seems to be a sort of fermentation colic. Other pathologic findings include chronic adhesive peritonitis, pneumonia, colon bacillus infections, tuberculosis, purulent spondylitis of the thoracic vertebrae with compression myelitis, and an abscess of the anterior thoracic wall and mediastinum. Among the parasites encountered were oxyuria, *Cysticerus fasciolaris*, *Trypanosoma criceti*, *Leukocytogregarina criceti* and *Sarcocystis criceti*. The hamster proved to be well adapted for experimental work, but caution is enjoined on account of the animal's tendency to bite. Its blood may be employed in complement-fixation tests, as a substitute for guinea-pig blood.

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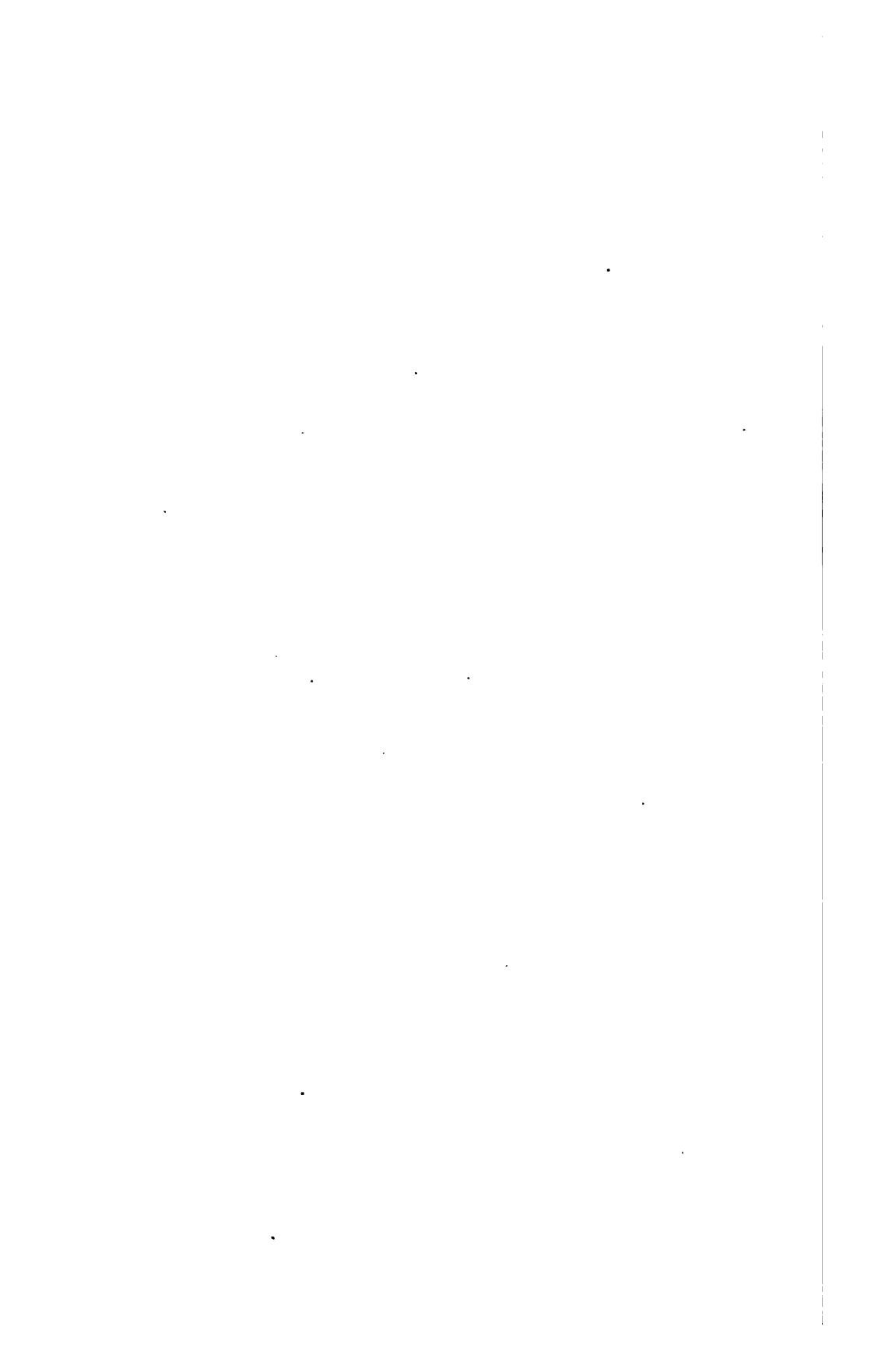
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**SECTION 1. ANATOMY, PHYSIOLOGY AND  
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**SECTION 1. ANATOMY, PHYSIOLOGY AND PATHOLOGY.**

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**Histology of the Motor Tracts in the Rabbit.**

*André Barbé, Rev. neurol., 28:1049, Paris, Nov., 1921.*

Rabbits have been selected because of the difficulty of studying the motor tracts in man. The regions included were the cortex, centrum ovale, internal capsule, peduncles, eminentia teres and medulla. In the cortex, there are 2 layers of pyramidal cells. The fibers sheathed with myelin are derived from the superficial layer. The myelin sheathing is complete about the third month. In the internal capsule, the fibers are grouped more compactly in proportion as the animal is older. The motor bundle occupies two-thirds of the convexity of the peduncle. In the eminentia, there is simply an increased number of fibers sheathed with myelin. The volume of fibers is also increased in the medulla, but the form and relations of the motor tract are not modified by the age of the animal.

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**Reticulate Fibers in the Normal Human Skin.**

*Hans Homma, Wien. klin. Wchnschr., 35:149, Feb. 16, 1922.*

The reticulate fibers, first discovered by Kupffer (1905) in the liver between the liver trabeculas, have since been found by other authors in the parenchyma of different organs. Homma has now discovered them, with the aid of the Maresch-Bielschowsky silver impregnation method, in the normal human skin. Some of the material was taken from cadavers and some from bits of skin removed at operation. They were demonstrated in the form of very fine fibers impregnated with black (1) around the cross section of the tubules of sweat glands, (2) in the walls of small blood-vessels, (3) in the subepithelial stratum. They can be definitely differentiated from collagen and elastic tissue.

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**The Physiologic and Pathologic Relations of the Lamellar Structure of Loose Connective Tissue.**

*E. Lagusse, J. de physiol. et de pathol. gén. 19:453, no. 4, Paris, 1922.*

Loose connective tissue, in man and other mammals, is composed of thin layers, superposed, which may slide upon each other, in greater or less degree. Scattered fibers hold the tissue together, and the layers are carpeted with fixed, infrequent and anastomosing cells. The structure permits formation of small interlamellar spaces, containing lymph. The circulation of the lymph is opposed by the thin barriers constituted by the walls of the spaces described. The lymph passes through these in accordance with the principles of osmosis. The rapidity of the flow depends upon the blood-pressure, composition of the tissue liquid, and, especially, upon the constitution of the connective (Sec. 1—Page 799)

tissue layers. The last factor is the most important, since the ever-varying tissue changes produce constant fluctuations in the permeability of the layers. The effects are immediately reflected upon local nutrition. By imbibition and adsorption, water, salts and toxic products may be prevented from circulating or may be allowed free flow. Arrest of the liquid in the tissue bears directly upon edema. The spaces constitute reservoirs which may receive any excess of water in the blood. The blood may relieve itself of such excess very promptly, and dependence upon the influence of the secretions is thus rendered unnecessary.

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**Two Neolithic Atlases.**

*L. Dubreuil-Chambardel, Bull. et mém. Soc. anat. de Paris, 18:488, Dec., 1921.*

In both specimens, the paraglenoid furrow is clearly evident. In most atlases, a crest extends along the external border of the glenoid cavity. The furrow is located between the crest and border of the cavity. It extends upon the upper surface of the lateral masses, at the expense of the external surface. Vascular foramina are present in the furrow. The latter is wider and deeper in the male. The description is illustrated by drawings.

(1a—298½)

(1a—298½)

**Investigations on the Weight of the Brain and Cranial Capacity According to the Method of Reichardt.**

*W. Panofsky and M. Staemmler, Frankfurt. Ztschr. f. Pathol., 26:519, no. 3, Wiesbaden, 1922.*

The Reichardt method determines the relationship of the weight of the brain to the internal capacity of the cranium by proceeding from the assumption that normally the difference between cranial capacity and brain weight amounts to 10% of the internal cranial space. The present investigation sought to test this assumption and to determine if there is a swelling of the brain in Reichardt's sense. Measurements showed that the average weight of the brain in males is 1386 gm., and in females 1230 gm. On an average, the difference between cranial capacity and brain weight during the middle age of life (between 20 and 50 years) amounts to 5.5%; after 50 years it increases for both sexes, amounting to 13% beyond 80 years. As these figures vary markedly from the measurements of Reichardt, the question arises whether there is a postmortem swelling of the brain. With the increase of time between death and necropsy, the difference between the cranial capacity and brain weight diminishes: After death the brain increases in weight, but the cerebrospinal fluid diminishes in amount; that is, the brain absorbs the cerebrospinal fluid and causes postmortem swelling of the brain. The brain weight in various diseases was then determined. Even though no definite conclusions can be drawn from a small number of cases of individual diseases, it can be stated that peritoneal diseases and the septic processes originating in the female genitals show a very slight difference, the acute infections and endocarditis then follow in order, and the septic dis-

eases show a distinct increase of the brain weight in relation to the internal capacity of the cranium. Postmortem swelling of the brain occurs in a varying degree in individual diseases. It is impossible to consider the postmortem swelling as constant in all diseases, and guarded interpretations must be made of the results of measurement of the brain and cranium in all necropsies done a long time after death, especially in those diseases in which the increase in postmortem weight is considerable, as in tuberculosis and tumors. If Reichardt's method is applied to individual cases, it is almost always impossible to determine the existence of brain swelling from the difference.

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(1a—299)

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**The Forking of the Spinous Process of the Cervical Vertebra and Its Causes.**

*H. von Eggeling, Anat. Anz., 55:33, Jena, Jan. 30, 1922.*

To answer the question, whether the forking of the end of the spinous process of the cervical vertebra is due to the action of the cervical spine, Eggeling compared the vertebrae and muscles of the throat of human beings, primates and lower apes. The forking of the vertebral spinous processes from the second to the sixth cervical vertebrae (at the sixth it is very variable) is distinct in Europeans. The forking starts at the cartilaginous apposition of the 2 halves of the spine: this shows that it is not individually acquired through the action of the muscles; but is the result of long hereditary influences. Its origin and conservation are due to the cervical interspinal muscles which are connected with the ends of the spinous processes. These muscles cause the dorsal flexion of the throat, its lateral movements and vertical rotation. The research material is too restricted to permit a decision as to whether these muscles are less developed in races which do not show a pronounced forking. Anthropoid apes only show a forking of 2 cervical vertebrae and the forking is found in chimpanzees most regularly. The other cervical vertebrae are long (short only in hylobates) and not forked; the cervical spine is less straight than that of human beings. Interspinal muscles are missing almost entirely, and the interspinal cervical muscle is very little differentiated. Dorsal flexion and vertical rotation of the cervical spine are limited, the first on account of the length of the spinous processes, and the latter because it is developed only after the vertebral column is straightened. In narrow-nosed apes the spinous processes are usually quite long, the ends are single; sometimes there is a little protuberance on the main points. The epistropheus of cercopithecidae is always forked, while macaques and pavians show such forking very rarely. The cervical spine is pretty straight, and has a distinct dorsal inclination. The spinous processes of broad-nosed apes are shorter, and, with the exception of the cebi, the free end of the spinous process of the epistropheus is provided with 2 small protuberances. The shape of the epistropheus resembles very much that of cercopithecidae. The cervical spine is bent slightly forward. In lower apes the development of the long interspinal muscles attains different degrees, and the short interspinal muscles are missing, except in cynocephali and the atèles. The semispinal cervical muscle of cer-

copithecidae is provided with a big protuberance for the epistropheus; insertions at the other spinous processes of the cervical vertebrae are very weak; while among other species they are distributed more evenly. A strengthening of the semispinal cervical muscles and of the interspinal muscles together with a shortening of the spinous processes only occurs in human beings; they both render the dorsal flexion easier. But these muscles also take part in supporting the head and in horizontal rotations of the cervical spine.

This proves the importance of the forking of the spinous processes for the erection of the body.

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(1a—300)

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**Incompletely Assimilated Last Occipital Vertebra in Man.**

*L. Bolk. Anat. Anz., 55:156. Jena, Feb. 28, 1922.*

In a very abundant material Bolk found some few cases with remnants of an independent rudimentary occipital vertebra, which was only incompletely assimilated. Either the precondylar or the postcondylar part of the occipital vertebra may appear as a free fragment. There were 2 cases in the first group: In 1 of them a small process extended from the median edge of the left condyle, but did not reach the right condyle; in the second case there were bone processes on the median edge of both condyles which did not extend far enough to come in contact. It is probable that in both cases the processes were connected by a ligament, so as to form a complete span. As this bone structure developed ventrally from the chorda dorsalis, it must have been only a hemapophysis of a vertebra and not the entire vertebra body. In the second group there were 3 cases in each of which a process of bone ran backward from a condyle. This partial independence of the posterior arch is combined with the manifestation of the anterior part of the occipital vertebra.

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(1a—301)

(1a—301)

**A Case of Double Common Iliac Arteries and of Double Inferior Portion of the Abdominal Aorta.**

*Hans Kobelt, Schweiz. med. Wchnschr., 52:253, Basel, March 9, 1922.*

At the necropsy of a man aged 46, who died of a fracture of the skull, the malformation described in the title has been found; it has not been observed before. In that case it had a clinical importance. A considérable atheromatosis had caused, in the left anterior iliac artery, an aneurysm and, starting from this place, an ascending thrombosis, which suppressed circulation in the arteries of both lower limbs; the second anomalous iliac artery had, however, maintained the circulation. The thrombus, parietally situated, ascended in the aorta for a distance of 5 cm.

The duplication of the aorta is easily explained by a persistence of the anlage, which at the very beginning is also double. The duplication of the iliac arteries may be explained, either by: (1) His's theory (Sec. 1—Page 802)

of penetration; (2) Rabl's theory of the formation of germinal prominences; or (3) P. Mayer's and Rückert's theory of the local genesis of embryonic vessels (recently advocated by Molliek).

(1a—302)

(1a—302)

**Comparative Physiology of Spermatozoa. II and III.**

*Ernst Gellhorn, Pflüger's Arch. f. d. ges. Physiol., 193:555, 576, Berlin, Feb. 22, 1922.*

The series by increasing effect, of K, Rb, NH<sub>4</sub>, Na, Cs, Li, for cations, and CH<sub>3</sub>COO, SO<sub>4</sub>, tartrate, phosphate, Cl, NO<sub>3</sub>, Br, I, for anions, which had been ascertained for the action of alkaline salts upon ciliated epithelium, has been rediscovered in various processes. Höber has assumed that this series expresses the action of the salts upon cell colloids. Nothing has been known concerning the behavior of spermatozoa in this respect. Isotonic salt solution paralyzes the motility of frog spermatozoa and shortens their life. The poisonous action diminishes with the concentration. Hence all salts were used in N/40 solutions. If only the moment of complete immobility is considered, or only the degree of mobility, i.e., the number of spermatozoa still moving in a given fluid, we obtain for cations the ascending series Cs, Li, Na, NH<sub>4</sub>, K, Rb. Considering the total course of the curves: Li, Cs, Na, NH<sub>4</sub>, K, Rb holds for *Rana temporaria*. Using *Rana esculenta*, the results were somewhat different. For the first series, Li, Cs and Na stand close together, as do NH<sub>4</sub>, K and Rb; in the second, Li, Cs, K with Rb, and Na with NH<sub>4</sub>. The cation series for guinea-pig spermatozoa is the exact reverse of that for *Rana temporaria*. Thus, while one series is nearly universally applicable to ciliated motion, the same is not true of the motility of spermatozoa. In cold-blooded animals, an anion group (tartrate, phosphate, sulphate and acetate), in which the spermatozoa retain their optimal motility often for hours, is contrasted with a paralyzing group, fluorid, thiocyanid, iodid and citrate, of which the first 2 are almost instantly fatal. Phosphate is the least injurious. Within the two groups, there are only slight differences between the various anions. Experiments with spermatozoa from cold-blooded and from warm-blooded animals give almost identical series, which closely resemble those for ciliated epithelium. Aside from the typical effect of limiting motility, certain cations cause morphologic changes in the spermatozoa: thus, K and Rb produce ring-formation, Fl and Pb produce coarse macroscopic agglutination, potassium with iron produce injury and dissolution into granules. The bivalent anions fluorid and thiocyanid, which momentarily paralyze the spermatozoa, do not alter the morphologic structure. These experiments serve to further support the hypothesis of a connection between physiologic ion action and an influence upon the cell colloids.

Great differences can be observed in the effect of alkaline chlorids upon the motility of the spermatozoa of *Rana temporaria*. Solutions of sodium, cesium and lithium salts preserve the motility for a long time, while the salts of potassium or rubidium will rapidly destroy it. This behavior might induce one to consider the possibility of inhibiting the toxic action of the one group of ions by a salt of the other group. Whereas heretofore, a neutralization of the poisonous effect within the

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series of alkaline metals could be determined only rarely and in slight degree, such neutralizing effect could be observed in tests with frog spermatozoa. If, for example, to a solution of sodium chlorid there is added potassium chlorid in amounts very small in proportion to the NaCl, a marked antagonism can be observed, which becomes less with increasing concentration of the potassium chlorid. Finally the curve of the saline mixture becomes identical with the NaCl curve, and in the end identical with that of KCl. A definite positive effect is indeed produced (i.e., the motility is increased and the life of the spermatozoa is prolonged) by the addition of KCl to a solution of NaCl, chlorid, as long as the molecular concentration of NaCl: KCl remains within the limits of 1:0.05 and 1:1. In view of the slight differences between these limits, no optimum can be defined. Lithium chlorid also neutralizes the toxic effect of KCl. Analogous to this division among the cations, the anions can also be divided into one group with poisonous effects, and another with more indifferent action. Tests were made to neutralize the poisonous effects of the sodium salts of the first group, by the addition of sodium salts of the second group. It could be shown that all anions of the second group: phosphate, tartrate, acetate and sulphate, can neutralize the poisonous effects of the halogens upon the motility of spermatozoa. Br and Cl can be more readily neutralized than I. The toxic effect of sodium iodid can be most readily paralyzed by secondary sodium phosphate. The same results were obtained with guinea-pig spermatozoa. Among the polyvalent cations, Ca, Sr, Ba, Cd, Zn, Mg, and Fe in the form of chlorids, Pb in the form of acetate, and Co as nitrate, were tested in their effect upon spermatozoa of *Rana temporaria*, and *R. esculenta*, as well as guinea-pig spermatozoa. Here also some cations, namely Mg, Ca, Sr, Ba, Fe, and Pb in suitable concentrations, exerted a strong antagonistic effect toward NaCl, while Cd and Zn did not show such action.

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(1a—303)

**On the Relations between Fertility and Nutrition. I. The Ovulation Rhythm in the Rat on a Standard Nutritional Regime.**

*Herbert M. Evans and Katherine S. Bishop, J. Metab. Res., 1:319, Feb., 1922.*

The authors attempt to lay a foundation for the study of aberration in ovulation due to defective diet and to establish the time of occurrence of the first estrum and the normal ovulation rhythm in rats maintained on a satisfactory diet. Comparisons between the behavior of animals on a generous and varied diet and animals on a standard diet showed no significant difference. In 80% of animals the first estrum occurs between the thirty-seventh and fifty-fifth day of life (average forty-seventh day) and three-fourths of all estrum cycles are five days long, about one-fourth lasting somewhat longer.

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(1a—304)

**The Formation of Tooth Roots.**

*Siffre, Bull. et mém. Soc. anat. de Paris, 18:523, Dec., 1921.*

An entire root mass, with single bulb, does not appear to exist in anthropoids. Instead, the bulb is divided into separate roots. Siffre (Sec. 1—Page 804)

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presents several specimens, showing root formation in anthropoids, neolithic man and contemporary man. Thin septums are produced by cellular proliferation arising in the free border of the neck of the tooth. The septums from the different teeth meet, dividing the bulb into chambers. The latter contain dentiginous centers. Each chamber represents a root. The persistence of the bulb in anthropoid apes does not precisely correspond to that present in prehistoric man; hence, hasty conclusions should not be drawn.

(1a—305)

**Phylogeny of the Epistriatum.**

*H. Kuhlenbeck and C. Kiesewalter, Anat. Anz., 55:145, Jena, Feb. 28, 1922.*

The epistriatum is the end stage of the median olfactory fibers; it is a secondary olfactory center, lies upon the optic thalamus and is reckoned as a part of the thalamencephalon. In addition to the olfactory fibers of the tractus bulbo-epistriaticus, the epistriatum in the higher forms of animals contains tertiary fibers from the olfactory cortex, the tractus cortico-epistriatici. In infants this group of nuclei changes its position and appears as the nucleus amygdalae, to which the taenia semicircularis or stria terminalis passes from the olfactory and parolfactory lobes in large half circles over the basal ganglia. Herrick, in studying a section of the basal ganglion of amphibia which he calls the amygdala, follows the relations of Jacobson's organ through the vomeronasal nerve to the bulbulus accessorius, which is the primary center of this organ, and further through the ventrolateral tract to the nucleus amygdalae, the secondary center and the end of the vomeronasal system.

This system is found only in diosomatic, not in monosomatic animals. Herrick's nucleus amygdala of the amphibia is identical with the part of the basal ganglion described as the epistriatum by Kappers, Röthig and Kuhlenbeck. Kuhlenbeck proceeds from the simplest brain in the mammalian series, the forebrain of amphibians, through the intermediary stage of the anurans to the powerfully developed epistriatum of the reptiles. In the amphibians and anurans it is still only slightly developed, but in reptiles it is powerfully developed, though to different degrees in different orders, and is one of the most striking characteristics of the forebrain of the reptiles. In this epistriatum a pallium and a basal part can be distinguished. The former is connected with the lateral cortical plate and consists of the anterior epistriate nucleus, the paraventricular nucleus, and the paraventricular part of the spherical nucleus. The basal derivatives are the rest of the spherical nucleus, and the superior basilateral nucleus. The epistriatum is a secondary olfactory center. The superior basilateral nucleus and a part of the spherical nucleus, the "amygdala" of Herrick are the end stages of the vomeronasal system.

(1a—306)

**The Development of Islands of Stomach Mucous Membrane in the Upper Part of the Esophagus from Their First Appearance in the Fetus to Birth.**

*Dora Boerner-Patzelt, Anat. Anz., 55:162, Jena, Feb. 28, 1922.*

Basing her study on an abundant material, Boerner-Patzelt de-  
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scribes the development of these mucous islands. Among 19 fetuses examined there were islands of stomach mucous membrane in 17 cases. Cells of type (1) described by Schridde were found in only 1 newborn infant. Large islands of type (2) were found in 2; in the other 7 cases there were only a few depressions. All 3 types probably began in the tenth to twelfth week, when the original 2 layered cylindric epithelium begins to differentiate. At this time groups of mucous cells of various size appear, which at first do not show any special preference for the lateral walls but are distributed quite uniformly over the whole surface. These mucous cells are very similar in form, structure and nucleus to true chief cells, but do not take mucous strains quite so well as the latter. The mucous cells on the anterior and posterior walls of the esophagus in almost all cases undergo slow retrogression. By the 16th week they are considerably shorter and form only the upper layer of a stratified epithelium. In the middle of the pregnancy the islands show a very active development. Later types (1) and (2) stop growing and only begin to develop again in postfetal life. Type (3) develops in the fetus to the form, if not to the size that it has in adults. The theory that these mucous islands are an ancestral organ is supported by the following 2 facts: their regular appearance in early embryonic life, and their greater frequency in the fetus than in the adult. This can only be explained by assuming that the mucous islands undergo partial or in many cases complete retrogression during fetal life.

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**The Hydrogen-Ion Concentration of Tissue Growth in Vitro.**

*M. R. Lewis and Lloyd D. Felton, Bull. Johns Hopkins Hosp., 33:112, March, 1922.*

The method of experimentation was by the observation of growth of cells from pieces of chick embryos transplanted into Locke-Lewis solution (Locke's solution plus chicken bouillon). The original solutions were made up at known H-ion concentration, and at the end of the experiment the H-ion concentration of the hanging-drop culture was determined by a special method. Growth in these tissue cultures occurred between pH 5.5 and 9.0, but the optimum was pH 6.8 to 7.0, i.e., lower than that of adult chicken blood, which is 7.4. The addition of dextrose to the medium was found necessary for growth longer than three days. Growth occurred in media containing as much as 5% dextrose, but the optimum dextrose concentration was 0.5 to 1.0%. The final H-ion concentration of the cultures depended upon the original amount of dextrose in the medium; the less the dextrose, the higher the H-ion concentration at the end. Cultures that failed to grow were usually slightly acid; those that grew well were usually neutral. These results are strikingly parallel to those found in the study of bacteria under similar conditions.

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**Quantitative Laws in Regeneration. III. The Quantitative Basis of Polarity in Regeneration.**

*Jacques Loeb, J. Gen. Physiol., 5:447, March 20, 1922.*

It has been previously shown by the author that the dry weight of shoots and roots produced under equal conditions of illumination, (Sec. 1—Page 806)

moisture, and temperature in sister leaves of *Brophyllum calycinum* varies approximately in direct proportion with the dry weight of the leaves; and that the same is true for the mass of shoots produced in small pieces of stem connected with a leaf. It is known that when a piece of stem is left in connection with a leaf, the mass of shoots produced by the leaf is less than when the leaf is completely isolated; Loeb has been able to show that in this case the stem connected with the leaf gains approximately as much in dry weight as the dry weight of the shoots and roots in the leaf would have been if the leaf had been completely isolated from the stem. The inhibitory influence of the stem on the shoot and root formation in the leaf was in this case due to the fact that when the leaf is connected with a stem, that part of the material which could have been utilized for the formation of new shoots and roots in the leaf now goes into the stem. The object of this paper is to show that the same simple quantitative relations suffice to account for the polar character of regeneration in a defoliated stem of *Bryophyllum*. The defoliated stem of a very large plant was cut into 5 pieces, each possessing 4 nodes, and the defoliated stem of a second plant was cut into 10 small pieces of 1 node each. The pieces were dipped with the base into the water and the large and small pieces were suspended in the same aquarium. The experiment lasted from September 27 to October 22. The shoots were then cut off and both shoots and stems were dried for twenty-four hours in an oven at about 100° C. The result was as follows: The dry weight of the 5 large stems was 13.670 gm., and the dry weight of their 16 shoots was 0.495 gm. The shoot production was therefore 36 mg. per gram of stem (all measured in dry weight). The dry weight of the 10 short pieces of stem with 1 node each was 2.880 gm., and the dry weight of the 19 shoots was 0.115 gm.; that is, 1 gm. dry weight of stem produced 40 mg. dry weight of leaves. These two figures, 40 mg. and 36 mg., agree sufficiently closely to show that under equal conditions the production of shoots of defoliated pieces of stem occurs in proportion with the mass of the piece of (defoliated) stem; or, in other words, the mass of shoots produced at the apex of the large defoliated stems is approximately equal to the mass of shoots the same stems would have produced if all the dormant buds of each stem had been able to grow out.

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Sources of Error in Radiophysiological Examinations.

H. Zwaardemaker, *Pflüger's Arch. f. d. ges. Physiol.*, 193:317, Berlin, Feb. 9, 1922.

It has been shown that potassium may be replaced in every perfusion fluid by other radio-active elements as desired, provided the dosage is in radio-equivalent quantities, as for instance, potassium salt to uranium salt in the proportion 10:1. In cold-blooded animals smaller amounts of potassium, as well as of other radio-active salts, must be employed in summer than in winter, while no difference exists in warm-blooded animals. A distinct and quantitatively measurable difference exists between the light and heavy metals of this series of mutually interchangeable members. Antagonistically, exogenous alpha radiation is ranged alongside the light metals and exogenous beta

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radiation alongside the heavy metals. Radiation and radio-active elements may be summated as regards their physiologic effects and their positive and negative signs. This radio-active equivalence applies to the automatism of the heart, intestine, uterus, frog's esophagus, to the control of permeability of the capillary endothelium, to the threshold impermeability of the glomerulus to glucose, and to the synapses between vagus and heart, as well as those between vasomotor nerves and vascular musculature. The various experiments were made on the hearts, intestine, uterus and vessels of frogs and rabbits as well as on edemas with both emanations and radiations.

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**The Electric Conductivity of Animal Tissues under Normal and Pathologic Conditions.**

*George W. Crile, Helen R. Hosmer and Amy F. Rowland, Am. J. Physiol., 60:59, March 1, 1922.*

By means of a special apparatus, illustrated and described in the article, the authors studied the electric conductivity of animal tissues. Sections of tissue were packed into small glass tubes of various sizes and the conductance capacities or cell constants of these tubes were determined by repeated measurements of their conductance when filled with 0.01 normal KCl, at the same temperature as that used for the tissue measurements. Special hard rubber containers were devised for the spinal cord. The results show the following order of the conductivities of the tissues studied: spinal fluid, bile, blood, voluntary muscle, cerebrum, cerebellum, liver and lung. The conductivity of the gray matter of the brain was found to be higher than that of the white matter. Exhaustion from any cause—surgical shock, insomnia, emotion, infection—was marked by diminished conductivity of the brain and increased conductivity of the liver. The immediate effect of activation appears to be an increased conductivity of the brain, tending later to decrease as the stage of exhaustion approaches. The tabulated results show this to be an immediate effect of physical injury; an early effect of the injection of diphtheria toxin; an immediate effect of the injection of adrenalin.

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**The Theoretic Response of Living Cells to Contact with Solid Bodies.**

*Wallace O. Fenn, J. Gen. Physiol., 4:373, March 20, 1922.*

In this paper the author discusses the theoretic behavior of an hypothetic fluid cell in contact with flat and curved surfaces, from the point of view of surface tension. An equation is derived for calculating the equilibrium position of the cell on a flat surface in terms of the surface tensions between the cell and the plasma, the plasma and the solid surface, and the solid surface and the cell. The same equilibrium is predicted from consideration of the contact angle between the cell and the solid body. The relative surface energy is calculated at various stages in the ingestion of a solid particle by a fluid cell 4 times as large in diameter, the author demonstrating that no particle will be ingested until the surface tensions are such that

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the cell would spread to infinity on a flat surface of the same substance. Here again the same equilibrium is predicted from considerations of the contract angle. The adhesiveness of blood-cells to solid substances is shown to be a pure surface tension phenomenon, but in most reactions between living cells and solid bodies the fluidity of the protoplasm is also a factor of prime importance. The frequent occurrence of adhesiveness as a property of cells in contact with solid bodies is due in part to the fact that, by so adhering, the surface area of the cell not touching the solid is decreased.

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(1a—311)

**Researches on the Permeability of Cells. Resorption from the Peritoneal Cavity by a New Method.**

*Y. Hara, Biochem. Ztschr., 126:281, Berlin, Feb. 15, 1922.*

Parenteral resorption is usually investigated from the peritoneal cavity, it being assumed that the capillaries are the essential factor in resorption. But in any event physiologic components participate in the resorption from serous cavities. Probably these components are situated in the endothelial cells of these cavities. A method was therefore devised which was to permit of the experimental alteration of a series of physiologic variables that might participate in the resorptive activity. It was also to permit experiments on an intact animal and their repetition as often as desired. With this object in view, a pigment was injected into the peritoneal cavity, namely fluorescein, because this substance rapidly enters the anterior eye chamber where it is easily detected by simple observation. Rabbits were employed as experimental animals and sterilized fluorescein-sodium solutions, at body temperature, injected. The anterior chamber of the eye was punctured by a fine needle in order to reduce the pressure. The entry of the pigment was observed in the dark room, the eye being illuminated locally by the Auer light. Under these conditions Ehrlich's line was seen descending from the upper pupillary margin. After a while the entire anterior chamber was filled by the luminous color. Fluorescein is resorbed from the peritoneal cavity very rapidly depending on the time received (1) for absorption of the fluorescein solution by the abdominal cavity, (2) for the transportation into the ocular vessels, and (3) for the discharge of the solution into the anterior chamber of the eye. To avoid errors, the method was so devised as to insure constancy of discharge into the anterior chamber. This is effected by always removing equal quantities of aqueous humor (2 c.c. in each experiment) previous to injection of fluorescein solution. Fine folds are observed on the surface of the cornea after the puncture. Time values were kept constant and noted carefully.

The experiments show that the rapidity of resorption is considerable but small in comparison to resorption from blood-vessels. The period required for the appearance of fluorescein in the anterior chamber is on an average 5 times as great. The chief difference in the time required by fluorescein to appear in the anterior chamber, according to whether the pigment was injected into a vein or into the abdominal cavity is governed by the time demanded for resorption by the endothelial cells of the peritoneal cavity. To what extent a physical or physicochemical factor influences resorption from the peri-

toneal cavity was investigated by means of a series of interferences. The physiologic part was excluded by local anesthesia of the peritoneum with novocain, with or without adrenalin, which was injected into the abdominal cavity or into the vertebral canal. A new method was employed here consisting in division of the splanchnic nerves. In all cases a very appreciable retardation of resorption was effected. Herein adrenalin exerted an influence by restricting resorption whereby the duration of action of novocain was lengthened. Physical conditions were improved by injections of hypertonic and hypotonic solutions into the abdominal cavity. In this case, also, the influence of physiologic factors, that is, the resorption capacity of the endothelial cells, is very probable. The injection of an isotonic sodium chlorid solution showed that the duration of resorption is not altered by injection of a 50% solution and that it is a matter of indifference whether the interval between sodium chlorid injection and injection of the 50% fluorescein solution amounts to two, or thirty, or sixty minutes. If the fluorescein injection took place a few minutes after the injection of hypotonic solution, the same great retardation occurred as in the case of the hypertonic solution. Three and a half minutes elapsed before the fluorescein appeared in the anterior chamber. The experiments point to a reduction of the resorative capacity in the endothelial coating of the abdominal cavity. The greatly retarded resorption (at times its complete disappearance) which is found after heavy loss of blood must likewise be referred to the diminished capacity for resorption of the peritoneal endothelial cells. Further, it appears from the experiments that an investigation of resorption from serous cavities should not be confined to resorption by the blood capillaries, but must extend to the physiologic resorption that depends on the living cells of the serous cavities.

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**The Influence of Hydrogen-Ion Concentration on Permeability of Dead Membranes, on Adsorption by Albumin Sols and on Exchange of Material in Cells and Tissues.**

*Albrecht Bethe, Biochem. Ztschr., 127:18, Berlin, Feb. 28, 1922.*

The acid dyes color parchment much more strongly in acid than in neutral or alkaline solutions. Most basic dyes behave in an inverse manner. Whether this adsorption depends mainly on a chemical or a physical process is unimportant. In the experiments short glass tubes were fitted and tied into the openings of the softened membranous envelope. The dye solution was put in large, wide-mouthed glass stoppered bottles. The dialyzing membrane, filled with water, floated in the solution. At various periods the contents of the membrane were carefully removed and compared colorimetrically with a specimen of the solution. The following basic dyes were examined: methylene-blue, Janus red, capri blue, the amphoteric pyronin and methyl-violet, which becomes anodic even at slight acidity. The acid dyes employed were cyanol, eriocyanin, light-green and thiocarmine. All of these acid dyes accelerate the diffusion compensation by the acid reaction. By alkaline reaction the same is considerably retarded. The behavior of methylene-blue and Janus red, among basic dyes, is just the opposite. Methyl-violet varies, its diffusion being most rapid in neutral and slowest in alkaline solution. The influence of the reaction on the

accumulation of dyes in colloids in the sol state was likewise investigated. Acid reaction in the cell interior increases the accumulating capacity for acid dyes and diminishes the dyeing capacity by basic dyes; conversely, with alkaline reaction, acid dyes effect little or no pigmentation; basic dyes are accumulated to a remarkable extent. The albumin solutions in the experiments were gelatin, serum and milk. If dyes diffused from an aqueous solution through parchment are brought into an albumin solution the dye is accumulated very strongly in the sol if an acid dye in acid solution is employed. On the other hand negative adsorption is observed with acid dyes when the solution is alkaline. Basic dyes behave in the opposite way. The process is reversible. The dyeing of animal and plant cells with different CH with basic, acid and amphoteric dyes also shows that hydrogen-ion concentration plays an essential part in vital dyeing. In the same way CH influences resorption and excretion from the intestine and kidney. The resorption of basic dyes is materially accelerated if acid is introduced simultaneously. Conversely the resorption of acid dyes is accelerated by administration of acids and diminished by alkalies. Under the same conditions in which resorption is favored or diminished, excretion from the kidney is accelerated or reduced. An alteration in the reaction of the urine accompanies the elimination of dye. The renal epithelium participates actively in this process. The active process obviously consists in the elimination of the acid, with which the elimination of the acid dye goes hand in hand, and conversely the vehicle for the elimination of basic dyes is the alkali passing into the urine through functional renal activity.

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**The Permeability of the Capillary Vessel Walls of Man.**

*Max Gänsslen, Münch. med. Wchnschr., 69:263, Feb. 24, 1922.*

Blisters were produced with cantharides plaster. The serum of one blister was collected with sterile instruments and its blood-sugar content was determined by Bang's method (determinations of iodin, chlorin and bromin also being made). The amounts of the same substances in blood were ascertained at the same time. A high-grade solution of glucose was then injected and the same determinations made for the serum of blisters which were produced subsequently as well as for blood taken simultaneously with the blister serum. Healthy persons produce blisters under normal conditions in twelve hours. In pathologic cases the formation of the blister serum was sometimes considerably accelerated and in other cases again it lasted much longer. In both conditions the formation of the blister serum took three to eight hours.

In 8 cases, 14 gm. glucose was injected intravenously while the blisters were growing. In 3 other cases 50-60 gm. glucose was injected in an empty stomach. In the first 8 cases increased sugar values were found only twice. The refraction values of the blister serum of 10 slightly affected patients averaged 45.7, and in 1 case of polyarthritis it reached 52-53 Pulfrich units. The blister serum of normal persons contained on an average 40.0 mg. nitrogen in 100 gm. of blister fluid, and blood serum showed similar values.

In chronic nephritis the blister serum showed distinctly higher fig-  
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ures. At the same time the blood serum showed partly higher and partly lower nitrogen content than the blister serum. In 1 case of acute nephritis 2 determinations showed normal nitrogen values in the blood, and somewhat higher ones in the blister serum.

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**Electric Charges of Colloidal Particles and Anomalous Osmosis.**

*Jacques Loeb, J. Gen. Physiol., 4:463, March 20, 1922.*

The author has previously shown that when solutions of different concentrations of salts are separated from water by collodion-gelatin membranes, electric forces participate in addition to osmotic forces in the transport of water from the side of the water to that of the solution. When the hydrogen-ion concentration of the salt solution and of the water on the other side of the membrane is the same, and if both are on the acid side of the iso-electric point of gelatin (e.g., pH 3.0), the electric transport of water increases with the valency of the cation and inversely with the valency of the anion of the salt in solution. Moreover, the electric transport of water increases at first with increasing concentration of the solution, until a maximum is reached at a concentration of about M/32; then upon further increase of the concentration of the salt solution the transport diminishes until a concentration of about M/4 is reached; then a second rise begins, which is exclusively or preëminently the expression of osmotic forces. The experiments previously described by Loeb show that Donnan equilibrium is the main source of the potential differences between solid gelatin particles and the surrounding liquid. However, experiments on the influence of salts on electric endosmose, cataphoresis, anomalous osmosis, and Quincke's current potentials suggest in certain cases at least a second source which is generally designated as adsorption potentials. The difference between the 2 kinds of potentials should be that while the potential differences (P. D.) due to the Donnan equilibrium depend on the ionization of the protein, the adsorption potentials should occur regardless of whether the solid colloid is ionized. Adsorption potentials should, therefore, be found just as well in the case of iso-electric protein where the protein is practically non-ionized as in the case of metal proteinates or protein-acid salts, while the potential difference due to the Donnan equilibrium should be restricted to the latter 2 forms of protein. The present object was to determine, on the basis of this idea, whether there exist, at the surface of solid gelatin, adsorption potentials in addition to potentials due to the Donnan equilibrium. For this purpose anomalous osmosis was used, by which is meant the superposition of electric forces over the purely osmotic forces in the transport of water through a membrane separating pure water from a solution of an electrolyte (or separating 2 different solutions of electrolytes). When both water and electrolytes are capable of diffusing through the membrane the difference in the mobility of the oppositely charged ions will cause diffusion potentials acting across the membrane. In this case the solution assumes the opposite sign of charge as the water. These potentials are designated as "*E*". There may be a second P. D. inside the pores of the membrane, between the solid wall of the pore and the liquid inside the

pore. This potential is called " $e$ ". The experiments show that the increase in the height of the transport curves with increase in the valency of the cation and inversely with the increase in the valency of the anion is due to the influence of the salt on the P. D. ( $E$ ) across the membrane, the positive charge of the solution increasing in the same way with the valency of the ions mentioned. This effect on the P. D. increases with increasing concentration of the solution and is partly if not essentially, the result of diffusion potentials. The drop in the transport curves is, however, due to the influence of the salts on the P. D. ( $e$ ) between the liquid inside the pores of the gelatin membrane and the gelatin walls of the pores. According to the Donnan equilibrium the liquid inside the pores must be negatively charged at pH 3.0 and this charge is diminished the higher the concentration of the salt. Since the electric transport is in proportion to the product of  $E$  times  $e$ , and since the augmenting action of the salt on  $E$  begins at lower concentrations than the depressing action on  $e$ , it follows that the electric transport of water must at first rise with increasing concentration of the salt and then drop. If the Donnan equilibrium is the sole cause for the P. D. ( $e$ ) between solid gelatin and watery solution, the transport of water through collodion-gelatin membranes from water to salt solution should be determined purely by osmotic forces when water, gelatin, and salt solution have the hydrogen-ion concentration of the isolectric point of gelatin (pH 4.7). This is practically the case when solutions of LiCl, NaCl, KCl, MgCl<sub>2</sub>, CaCl<sub>2</sub>, BaCl<sub>2</sub>, Na<sub>2</sub>SO<sub>4</sub>, MgSO<sub>4</sub>, are separated by collodion-gelatin membranes from water; however, when the salt has a trivalent (or tetravalent?) cation or a tetravalent anion, a P. D. between solid isolectric gelatin and water is produced, in which the wall assumes the sign of charge of the polyvalent ion.

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**The Distribution of Water and Ions in the Organism.**

*Heinrich Reichel, Biochem. Ztschr., 127:322, Berlin, Feb. 28, 1922.*

The phenomena of the distribution of solutions of certain poisons through the various constituents of the cells can be comprehended only on the assumption that cell fibers rich in albumin are very deficient in water and free from salt. On the basis of water-deficient and salt-free colloidal fibers it is possible to explain, also, the physiologic intumescent, toxic and fermentative effects of acids and combinations with salts. In these processes electrolytic dissociation in the colloidal phase is ascribed to the acid part combined with albumin. As the acid albumin solutions that give a neutral reaction with an indicator change to an acid color on the addition of neutral salts, this was looked upon as a proof of a reaction between the colloid and the salt, which conflicts with former contentions. In a simple experiment, serum coagulated by heat, in a finely chopped state, replaced liquid horse serum and was added to the test solution containing sodium chlorid 0.2, semi-normal hydrochloric acid 4 c.c., and methyl-orange 10 drops. The initially red liquid lost its intense color rapidly and became pink, exactly as would liquid horse serum. The suspensions assumed a yellow color and this was not attended by acidification of the solution. The contrary color change seems to depend on the restitution of the dye from the suspensions to the liquid under the influence of the neutral salt. Acid-

ification is therefore merely apparent and is simulated by the system's diphasic character. Hence it is unnecessary to seek an explanation in a reaction between colloid and neutral salt.

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**Intumescence of Subcutaneous Tissue.**

*P. Morawitz and G. Denecke, Biochem. Ztschr., 127:47, Berlin, Feb. 28, 1922.*

In accordance with Kohnheim's earlier researches, edema in kidney diseases is referred to injury to the vessels, that is, to the vascular endothelium, which leads to increased effusion of fluid into the tissues. If absorption of the fluid is disturbed simultaneously edema must result. On the other hand, Fischer's theory assumes an alteration of osmotic pressure of protoplasmic substance under the influence of physicochemical factors. For this reason it seemed desirable to undertake experiments for determining the behavior, on the one hand of an artificially intumescent colloidal system in the tissue of healthy individuals, and on the other its behavior in animals in whom an edematous tendency exists. As an artificially intumesced system, calculated to effect the exchange of fluid with the tissue fluids, the authors employed 20% agar which was prepared with Ringer's solution and poured into Petri dishes. From this, tablets of 0.1 gm. were compressed. These tablets were allowed to soak twenty-four hours in Ringer's solution, weighed, and then sunk in rabbits' subcutaneous cellular tissue. The cutaneous wound was closed with Herff's wound clamp. After twenty-four hours the wounds were opened and the tablets removed and weighed. Such experiments were carried out with normal animals as well as on those in a state of initial edema. Uranium nitrate and ligation of the ureter favored edema. From the tabulated results it appears that artificial colloidal systems (agar tablets saturated with serum or Ringer's solution) always diminish in weight in twenty-four hours when submerged in normal subcutaneous tissue. In subcutaneous tissue of animals poisoned by uranium or with ureters ligated, the tablets increase and never decrease in weight. It seems improbable that alterations in hydrogen-ion concentration or of osmotic pressure can be held responsible for the varying behavior of intumescent and colloidal systems in the subcutaneous tissue of normal and edematous animals.

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**The Reciprocal Relationship Between Blood Plasma and Tissue Fluids, Particularly Aqueous Humor and Cerebrospinal Fluid.**

*J. de Hahn and S. van Greveld, Biochem. Ztschr., 124:172, Berlin, Nov. 21, 1921.*

In regard to the sugar content it was shown in a former work that the aqueous humor and the cerebrospinal fluid behave like a dialysate of blood plasma. Experiments were conducted to determine whether the same fairly great permeability exists also for other crystalloids and whether this is the same for both fluids. For this purpose, 2 easily demonstrable bodies were used: potassium fluorescein for the aqueous humor and potassium iodid for the aqueous humor and the cerebrospinal fluid.

The experiments showed that the pigment did not diffuse through dead membranes, provided it was dissolved in blood serum. A comparison of the behavior in *in vivo* and *in vitro* was made: a 1:20,000 solution of potassium fluorescein in 0.9% saline solution completely penetrated an ultrafilter; when the same concentration in the blood serum of a rabbit was employed, the largest part of the pigment was left on the filter and the concentration was much less in the albumin-free filtrate, varying from 1:100,000 to 1:300,000; the same results obtained when the dialysis proceeded under pressure. On comparing these figures acquired *in vitro* with the processes in the eye, there was a marked uniformity: with a plasma concentration of 1:20,000, the aqueous humor of the rabbit showed pigment values of 1:500,000, somewhat more than an hour after about 150 mg. potassium fluorescein was injected intraperitoneally. Fluorescein injected into the body passes into the aqueous humor in the same manner as could be demonstrated *in vitro* with ultrafiltration. The membranous system which divides blood and aqueous humor behaves accordingly like a dialyzer, impermeable to colloids. The aqueous humor and the cerebrospinal fluid behave uniformly as far as remaining uncolored by pigments is concerned, but from their permeability by iodin salts, the conclusion can still be drawn that the described membranes are not alike in nature.

It is well known that methylene blue, immune bodies, ferments, urotropin and chloroform rapidly enter the cerebrospinal fluid. An isotonic solution of potassium iodid was injected into an adult rabbit in such amounts, that the plasma concentration remained for several hours at about 1:1000: at the end of the experiment, blood, cerebrospinal fluid and aqueous humor were aspirated as nearly simultaneously as possible. For the iodin determination .2 c.c. of the fluid was used, the iodin was freed with acid and the iodin content was determined colorimetrically. The blood was previously freed of albumin. The experiments showed that there was a very rapid diffusion into the aqueous humor where an equilibrium had been established with the blood plasma simultaneously; and only much smaller amounts of iodin were present in the cerebrospinal fluid. Parallel experiments showed that no demonstrable amounts of iodin were present either in the brain tissue or in the muscle flesh, whereas the concentration in the blood plasma and in the aqueous humor amounted to about 1:2000. The reaction was negative in the cerebrospinal fluid. This shows that the exceedingly low concentration of iodin in the cerebrospinal fluid in comparison to that in the blood plasma and in the aqueous humor must be attributed to a lesser permeability of the particular membranes in the brain for iodin. This does not involve an absolute retention, but only a retardation of the diffusion. With potassium fluorescein it is a matter of an absorption effect of the pigment upon the plasma colloid, whereas the iodin salts in the blood serum are not appreciably bound to the colloids. The rapidity of diffusion of the iodin salts is much greater in the aqueous humor of the rabbit than in the cerebrospinal fluid. Accordingly potassium iodid behaves differently from glucose in this respect. There is no great affinity of iodin for brain tissue.

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**Exchange Processes between Blood and the Tissues. I. The Influence of Diuretics.**

*Julius Bauer and Berta Aschner, Deutsch. Arch. f. klin. Med., 138:270, Leipzig, Feb. 21, 1922.*

Much attention has recently been paid by workers in biology to the processes of exchange going on between blood and tissues. These exchanges are so interesting and so manifold that they can hardly be overlooked. The current of exchange is in both directions in relation to the capillary walls but there is as yet no knowledge of the fine mechanism of regulation of these continuous and precise apparatus. For several reasons this knowledge is of great interest. In their investigations the authors injected diuretics intravenously, after a period during which no medicinal substances were given and in which there were no important changes. The blood used for examination was removed from a vein at the bend of the elbow but there was no preliminary stasis of the blood current. Sufficiently large quantities of blood may be withdrawn after a little practice without stasis of the venous flow. The experiments were always made in the morning while albumin was determined with Pulfrich's dip refractometer and the NaCl content was determined by the very exact iodin method of McLean and Van Slyke. The experiments showed that theocin, euphyllin and theophyllin caused a concentration of the blood during which the diuresis may become considerable. The albumin content of the blood increases with euphyllin but the NaCl content decreases. This is of no importance in the diuretic effect. Diuretin causes hydremia; it may cause hydremia without diuresis and it does not change the NaCl content of the blood. The change in the NaCl content and the occurrence of hydremia are not to be considered as conditions for diuresis. The albumin and NaCl content of the serum is nearly constant even when a hypertonic solution is injected in the circulation. Even strophanthin causes diuresis by extrarenal effects, producing a dilution of the blood if given intravenously. The selective action of diuretics can be due only to a specific renal effect and to a change in the colloidal condition of the blood, even though there are undoubtedly demonstrable extrarenal factors.

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**The Osmotic Effects of Intravenous Injections of Sugar under Varying Conditions. II.**

*Max Bürger and Erich Hagemann, Ztschr. f. d. ges. exper. Med., 26:1, Berlin, Jan. 20, 1922.*

In a series of tests the blood has been examined after injections of sugar, by means of the U-tube hemocrit, by cyroscopy, by the conductivity test and by refractometry. Preliminary tests *in vitro* had shown that the addition of sugar diminishes the conductivity of ion-dispersed solutions. Infusion of sugar solutions *in vivo* causes an influx of tissue fluids into the circulation, which produces a hydremic plethora, accompanied by increased blood pressure, but without any considerable diuresis. The hydremia after the injection of sugar solutions is not the same in the capillaries as in the veins. This is explained by assuming that the capillaries mechanically respond to increased

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osmotic pressure by a countercurrent of tissue fluid poor in ions, mols and albumins. In a prevenous (postulated) vascular area, plasma is again given off to the tissues by transudation, whereby the amount of circulating blood is again diminished.

Analogous conditions prevail in dropsy, but the processes run a much slower and more intense course. Sodium chlorid is in a class by itself, there being instances in which movements of NaCl take place which appear directly to contradict the laws of osmosis and diffusion. In such cases we must assume a physiologic activity of the cell membrane.

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**Reciprocal Action of Simultaneous Stimulation of Several Cutaneous Senses. I. The Influence of Cutaneous Temperature upon the Threshold of Tactile Sense.**

*Rudolf Allers and Fanny Halpern, Pflügers Arch. f. d. ges. Physiol., 193:595, Berlin, Feb. 22, 1922.*

The threshold of tactile sense was measured by means of a hair which was permitted to fall from a variable height, while at the same time the skin was warmed. There was a lowering of the threshold, i.e., an increased sensibility, with an increase in cutaneous temperature, up to an optimum. When the temperature was raised beyond this, the sensibility became less marked. This result is dependent upon whether the initial temperature of the skin is higher or lower. Similar curves may be obtained when active or passive hyperemia of the skin is produced. Passive tension of the skin also influences the tactile sensibility in such a manner as to cause it to pass through a minimum; further increase of tension produces a renewed diminution. From the minimum produced by tension, the threshold may be further lowered by heating. Relaxation of an abnormally stretched skin, such as occurs after tapping in ascites cases, shows the reverse effect: originally low tactile sensibility increases to an optimum, and finally diminishes about the time when fine folds and wrinkles in the skin render the cutaneous relaxation visible. The varying tension of the skin is probably largely, if not entirely, responsible for the changes in tactile sensibility.

An analysis of the factors concerned (diminished thickness of the skin, diminished tendency to deformity by increased tension, and the simultaneous stimulation of several sensory apparatus) show that an interpretation of these results is difficult if one maintains that tension stimuli and pressure (tactile) stimuli are of the same nature. A possible explanation might be furnished, if it were agreed to assume a qualitative inequality of the pressure and tension stimuli, since a diminution of the threshold has been described for the simultaneous action of disparate stimuli. Such an influence must be regarded as chiefly psychic.

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**The Ganglion Cell Is not the Anatomic Basis of Automatic Heart Action in Vertebrates.**

*Hering, Pflüger's Arch. f. d. Physiol., 193:621, Berlin, Feb. 22, 1922.*

When claiming that the ganglion cells of the heart are the  
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initiators of automatism of the vertebrate heart, Tigerstedt did not do justice to the important fact that the intracardial accelerator nerves of the heart are postganglionic fibers. This proves that the ganglion cells are not the basis of the automatic action of a vertebrate heart isolated from the extra cardiac nervous system. It is also useless to draw upon the findings made upon the limulus of heart. There should be a sharp differentiation between the neurogenic theory and ganglion cell theory. The clearness of representation suffers when this is not done (Tigerstedt). So far as the ganglion cells are concerned, facts point directly to an extracardial, not intracardial, automatism. Its myogenic nature has not been conclusively established. But the alternative is: myogenoneurogenic and not myogenogangliogenic.

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**The Action of Phosphate on the Heart.**

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*H. Straub, Biochem. Ztschr., 127:255, Berlin, Feb. 28, 1922.*

The progress in muscular physiology depends on the fact that skeletal musculature contains unmedullated sympathetic nerves in addition to medullated spinal nerves and further that, besides true tetanus, there exists a tonic contraction, i. e. a permanent shortening without internal work or oxygen consumption, and without active current or muscular tonicity. Also, the capacity for work of the muscle depends, not on the oxidation, but on an anoxybiotic decomposition of sugar. During work lactic acid is formed from carbohydrate while oxygen is formed only during recovery by the oxidation of a part of the lactic acid. Finally the decomposition of carbohydrates proceeds which phosphoric acid occurs in the organism, calcium phosphate is the most important and it seemed reasonable to assume relations between calcium phosphate and muscular phosphate. On the heart, calcium salts, after initially increasing the degree of contraction, produce imperfection of the diastole, namely of the recovery phase. The contraction of the cardiac muscle, as induced by toxic doses of digitalis glucosids, may be accelerated by addition of calcium. It is possible that phosphoric acid, which is otherwise paired with glucose, is here combined with calcium and that it is thereby withdrawn from its true function for muscular recovery. Actually, a heart brought to standstill with digitalis was made to resume its beating by phosphoric acid.

The action of phosphates on the healthy, on the insufficient and the poisoned frog's heart was investigated. Alkaline phosphate was found to act more favorably on the insufficient heart than acid phosphate. All experiments showed that hearts injured in their activity are again rendered adequate. This action is explained by assuming that phosphate, as an important connecting link in muscular carbohydrate exchange, increases the dynamic functional capacity and thereby also the capacity for resistance to any injuries, mechanical or toxic. That appears also from a reversal of the experimental procedure in which, for instance, following previous application of phosphate a threefold adrenalin dose is required to produce poisoning. Experiments were also conducted on heart patients, 200 c. c. 2% sodium phosphate solution being injected (pH 9.0). Before and after injection the pulse, blood pressure, respiration, sphygmograph and subjective symptoms (Sec. 1—Page 818)

were noted. In all these clinical observations on heart patients the cardiac symptoms (pressure over the chest, dyspnea) improved. The objective improvement persisted for days. From the favorable action of phosphate on subjective symptoms in heart patients, and from the therapeutically important fact that the  $\text{PO}_4$  promotes the action of cardiacs, the action of phosphate may be assumed to reside in the requirement of  $\text{PO}_4$  by the cardiac muscle as a working substance, in order to perform its dynamic functions with the help of carbohydrates. Glucose appears to be present in the body at all times in sufficient quantity, and if phosphate be now added the possibly disturbed equilibrium is restored. The equilibrium: hexose-diphosphoric acid  $\rightleftharpoons$  glucose + phosphoric acid is obviously of extraordinary importance in animal and vegetable economy. The rôle of phosphate ions in intermediate metabolism is peculiar. Organic phosphorus is taken up, inorganic phosphates are eliminated. But the phosphate ion, unlike the similar sulphur, is not effete matter, but a component of osseous tissue. And, further, phosphorus possesses relations to skeletal muscles and, as is shown by these researches, to the cardiac muscles.

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**Direct Demonstration of Conduction of Stimuli along the Muscles in the Heart of Vertebrates.**

*L. Haberlandt, Med. Klin., 18:276, Vienna, March 2, 1922.*

Haberlandt's experiments have shown that heart apexes, which were clamped according to the method of Bernstein, showed that the end fibers of the intramuscular nerve plexus were degenerated after three or four weeks, in spite of the fact that the conduction of stimuli was still retained in this time. This was done in the frog; Haberlandt considers this the only direct demonstration of muscular conduction of stimuli in the hearts of vertebrates. Such heart tips with degenerated ends of the nerve fibers showed no effect with electric or chemical stimulation of the intracardial vagus or accelerator nerves. This is due to the fact that it is impossible to produce a nervous influence on the motor function of the heart muscle after degeneration of the end apparatus of the regulatory nervous system of the heart. These experiments show that the end fibers of the nerves are really degenerated after a time. Therefore the physiologic peculiarities of the cardiac apex, such as irritability, refractory phase and conduction of the motor stimuli, are pure muscular manifestations and are independent of the net of intracardial nerve ends. The latter have a regulatory function exclusively, while the muscle is independent of the nerves for the conduction of the other stimuli under discussion.

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**On the Relation of the Vagus Nerves to the Action of Sinus Venosus, and on the Nature of Inhibitory Action of the Heart Beat.**

*Kenta Ohmori, Japan Med. World, 2:61, Tokio, March 15, 1922.*

In these experiments, toads' hearts were used, stripes of muscle of the sinus venosus being prepared. By using Engelmann's suspension method the action of the muscle was traced by myograph. Tetanic (Sec.1—Page 819)

stimulus was applied on the trunk of the vagus nerve outside of the heart, or the peripheral end of the vagus was directly stimulated by muscarin. Ohmori concludes that the automatic center of the heart beat is not situated in the contractile substance of the muscle. Whatever its mechanism may be, there is no question that it lies between the muscle and the vagus nerve. In this special mechanism, autochthonous stimulation is produced and brings about the normal rhythmic beats. Excitation of the vagus causes frequent dissimilation stimuli at the automatic center, which interfere with the rhythm, and produce dissimilation paralysis. According to the relation of the rhythm to the primary stimulus and the frequency of the extrinsic stimulus, there is a time when there is no impetus and the heart muscle is relaxed (pause), or the rhythmic action becomes slow (negative chronotropic action), or there is accelerating action (positive chronotropic action). The decrease of contractility, or negative inotropic action, may be due to the fact that before the automatic center has started the stimulating action, the muscle has lost a part of its excitability.

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**Experiments on Gaseous Exchange and Minute Volume of the Heart in Massage and Passive Movements.**

*G. Liljestrand and M. Stenstroem, Biochem. Ztschr., 127:218, Berlin, Feb. 28, 1922.*

The question of the action of massage and passive movement on gaseous exchange and minute volume of the heart was studied by means of auto-experiments. Respiratory metabolism as well as respiration frequency during standard conditions were determined by experiments of brief duration. The personal noxious space was estimated by Krogh and Lindhard's method, the extra noxious space of valve and mouth piece was known. Alveolar  $\text{CO}_2$  tension could therefore be calculated from the respiration experiments. Immediately after the last respiration experiments several estimations of venous carbonic acid tension were carried out by Fridericia's method. As the  $\text{CO}_2$  absorption curve of the blood had been obtained by Krogh and Liljestrand's method, the  $\text{CO}_2$  content of the blood with arterial and venous  $\text{CO}_2$  tension could be determined. The minute volume was then obtainable by simply dividing eliminated  $\text{CO}_2$  by the difference between venous and arterial  $\text{CO}_2$  content. After the rest experiments further experiments were then undertaken in exactly the same manner with muscular massage and abdominal massage, and with passive movements.

The experimental tables show that frequency of respiration was increased during muscular and abdominal massage, as well as during passive movements. Oxygen intake was increased slightly. The minute volume of the heart was found to be independent of massage in these experiments. It appears, therefore, that the action of massage and passive movements on the blood flow in muscles in healthy individuals must be comparatively slight.

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**Studies on the Responses of the Circulation to Low Oxygen Tension. VI. The Cause of the Changes Observed in the Heart During Extreme Anoxemia.**

*Charles W. Greene and N. C. Gilbert, Am. J. Physiol., 60:155, March 1, 1922.*

In this work progressive anoxemia was induced in 21 animals, in a total of 41 experimental tests, to determine the course of physiologic events. Dogs were used exclusively and the anoxemia induced after chlorethane anesthesia either alone or combined with ether. The rebreather method was employed by an apparatus of small size suited to animals of about 7 to 10 kilos body weight. Changes in the general blood pressure were measured by a mercury manometer, taking the reading from the carotid artery. Respiratory rate was recorded by the movements of the spirometer. This apparatus records the progressive changes in volume of the enclosed air, thus giving a measure of the variations in rate and amount of oxygen consumed. Electrocardiograms were taken at intervals of about 4 minutes beginning with the normal. A continuous electrocardiogram was taken from a late moment in the precrisis stage through the entire postcrisis stage and till the ending of the experiment by death of the animal, or by recovery following artificial respiration. An analysis of the enclosed air in the rebreather chamber was made at the termination of the experiment.

After anoxemia is pushed to the stage of suppression of the respiratory movements there still remains a considerable interval during which artificial respiration quickly revives the animal. Revival permits several tests on the same dog. Since the authors' primary purpose was to determine the mechanism of the effects of anoxemia expressed by changes in the heart, they made the tests in 4 groups: (1) with the vagi intact; (2) with both vagi cut; (3) after atropin; and (4) with the vagi cut at the moment when advanced responses are in progress in the heart.

In summarizing the observations from blood pressure records obtained by carrying anoxemia to the complete limit of stopping respirations and heart beats, the authors state that the reactions of the respiratory center of the medulla become at first slow, then cease. When lack of oxygen is pushed to the death there is a phase during which the respiratory center does not receive enough oxygen to maintain its normal discharges. The inhibitory centers controlling heart rate do not fail as early as the respiratory mechanisms. This is indicated by the appearance of the maximal cardiac slowing after the respiratory center has ceased. The cardiac slowing in the early postcrisis stage is not due to cardiac failure, i. e., muscle and bundle failure, since it does not occur if both vagus nerves are previously cut. Direct cardiac anoxemia is not adequate to suppress heart activity until from three to five minutes after respiratory failure. The extreme slowing occurring after respiratory failure is promptly removed only after cutting both vagi. The authors show that there is an interval of from three to five minutes following respiratory failure during which cardiac beats are maintained. The rate becomes progressively slower. At any moment during this interval a supply of fresh oxygen by artificial respiration is adequate promptly to recover circulatory and respiratory efficiency and remove the vagal inhibition.

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The Determination of the Circulation Time in Rabbits and Dogs and Its Relation to the Reaction Time of the Respiration to Sodium Cyanid.

A. S. Loevenhart, B. H. Schlovowitz and E. G. Seybold, *J. Pharmacol. & Exper. Ther.* 19:221, April, 1922.

The average circulation time from the marginal ear vein to the opposite marginal ear vein in the rabbit was found to be 4.71 seconds. The average circulation time in the dog from external jugular to external jugular vein was 7.8 seconds. The average reaction time of the respiration to sodium cyanid on injection into the marginal ear vein in rabbits was 3.97 seconds. The average reaction time of the respiration to sodium cyanid when injected into the external jugular vein in dogs was 8.66. A determination of the reaction time to sodium cyanid, either in the rabbit or dog, gave a figure which was within one second of the complete circulation time. In the rabbit the reaction time to cyanid was 84% of the complete circulation time. In the dog the reaction time was 111% of the circulation time.

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(1a—326)

The Fluctuations in Capillary Circulation.

Wilhelm Hagen, *Ztschr. f. d. ges. exper. Med.* 26:80, Berlin, Jan. 20, 1922.

On the basis of cinematographs of capillary reactions to heat and adrenalin, the author believes that the capillaries do not possess a separate vasomotor system, since the nerve fibers reaching the capillaries radiate into the surrounding tissue. In opposition to the explanation of capillary reactions due to reflex arcs, he cites cases from human pathology showing that fainting (central impulses) suppressed capillary reactions. In his experiments with quinin, he considers solely the inhibitory action. Seasonal variations play a part in the production of dermographia alba, whereas this is not true of adrenalin reactions. The author upholds his observations on adrenalin, and also his theory of stasis. Concerning the quantitative rôle of the factors involved, he has become convinced during a visit to Krogh, that adventitious cells of the capillaries, according to Rouget and Meyer, do actually exist.

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(1a—327)

The Physiology of the Nail-Bed Capillaries in Normal Individuals.

S. S. Chou and W. Dieter, *Pflüger's Arch. f. d. ges. Physiol.*, 193:459, Berlin, Feb. 9, 1922.

In 500 normal individuals measurements with the ocular micrometer showed a fairly constant width of the capillaries (arterial branch 0.01—0.03 mm.; venous branch up to 0.05 mm.) but considerable variations in the length of the loops in the separate digits. A comparison of the average values distinguishes 2 groups: (1) comprising 60%, of 160—400 microns; and (2) comprising 30% of 400—550 microns. The length of the capillaries depends on the absolute length of the loop and on the conditions of visibility (nature of the epidermis, moisture content of tissues, position of capillaries with regard to direction of vision, intensity of source of light). Occupation, meteorologic conditions and skin hygiene play a part. In normal

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individuals, a strip of skin 3.0 mm. in length and 0.15 mm. in width has 30-34 loops. Following removal of the uppermost cutaneous layers with barium sulphid, inflammation ensued accompanied by tense filling of the capillaries with distinct contour markings, rapid flow and widened lumen. Adrenalin solution (1:1000) applied to these portions of skin caused no material alteration of the blood flow even with prolonged action; the capillaries were filled less tensely and appeared narrower but showed no stasis that would indicate angiospasm. The action of adrenalin was not altered by removal of the epithelium owing to a burn blister. But this action cannot be referred to an influence on the capillaries because an influence on the arterioles is not excluded. The same applies to the results after mechanical and thermal stimulation. Facts are wanting, therefore, that would point unconditionally to active capillary contractility although the latter may have a share in the phenomena.

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(1a—328)

**Action of the H-Ion Concentration upon Blood-Vessels, with Special Reference to the Degree of Buffering of the Perfusion Fluid.**

*Edgar Atzler and Gunther Lehman, Pflügers Arch. f. d. ges. Physiol. 193:463, Berlin, Feb. 22, 1922.*

The authors had previously determined that both H ions and OH ions exert a contracting action upon the blood-vessels as soon as the concentration has exceeded a certain value; this titer is lower for the OH ions than for the H ions. Since the normal H value of the blood lies within the limits of activity of OH ions, the blood-vessels are in the state of contraction designated as "hydroxyl contracture" under physiological conditions. Acid products of metabolism diminish this hydroxyl contracture and thus at first dilate the circulatory passages. The same phenomenon can be observed when a slightly acidulated perfusion fluid is passed through an animal, unless nervous mechanisms interfere. The physiological hydroxyl contracture remains even when a neutral slightly buffered or unbuffered solution is circulated through the animal before the actual perfusion experiment. The degree of buffering denotes the amount of resistance shown by the H-ion concentration of a solution to the addition of acids or alkalis; this degree is the higher, the more cubic centimeters of a normal acid must be added to 100 c. c. of the buffer solution to alter its H ion concentration by a power of 10. A solution of gum-arabic in Ringer's fluid, which was used to circulate through the animal, exerts a buffer action owing to its content of arabinic acid, since this acid possesses only a low dissociation constant. With such perfusion the optimum for the circulatory system lies within PH 5-7. If PH is less than 5, or more than 7, the vessels will contract. The degree of buffering may be varied by the addition of salt solution, or primary and tertiary sodium phosphate. By this means any desired H-ion concentration in the required PH limits could be produced in 3 degrees of buffering. The degree of buffering was shown to be one of the factors in the production of blood-vessel contraction; i. e., the latter does not depend solely upon the degree of H-ion concentration. A strongly buffered solution does not act within the PH limits 5.65 - 6.6, while the inactive zone

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for a weakly buffered solution lies between PH 4.2 and 7.45. For an unbuffered solution it lies between PH 2.9 and 9.35. This can in part be explained by the fact that the tissues of the frog possess the power to alter a perfusion fluid of abnormal H-ion concentration so that it approaches the reaction of the blood. The organism diminishes the acidity of an acid fluid and renders an alkaline solution less alkaline. This approach is the more nearly perfect, the lower the degree of buffering of the perfusion fluid. This property of the frog organism can even be expressed in figures.

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(1a—329)

### The Effect of Vascular Stimuli upon the Elasticity of the Arterial Wall.

J. Schleier, *Pflügers Arch. f. d. ges. Physiol.*, 193:610, Berlin, Feb. 22, 1922.

If one compares the amount of effluent in perfusion of a frog's leg under steady pressure with that resulting when rhythmic pressure is employed, the latter method is found to yield the greater quantity, even without the aid of vasomotor drugs. This superiority may be founded on physiologic or on physical causes: the assumption of an automatic action of the blood-vessels is unnecessary if physical causes can be demonstrated. Fleisch has drawn upon the elasticity of the vascular system for an explanation, since this elasticity, with increasing pressure, diminishes the resistance of the blood channel more than is proportionate to the pressure. The present investigation extends to the alterations in elasticity of the vessel under the influence of adrenalin or barium chlorid. The hind legs of winter frogs were used. The pressure and the intensity of a current of Ringer's solution entering the abdominal aorta were measured by a torsion-spring manometer and a small registering water-meter. A comparison between the perfusion of normal vessels and vessels under the influence of adrenalin or barium chlorid shows that under normal conditions the volume of current rises very little more than corresponds to the pressure, while the rise is very much higher in stimulated vessels. This increased elasticity of the channel of the blood current, which causes the disturbed relation between pressure and current, is not a specific action of vasoconstrictor drugs; the vessels are the more elastic the higher their tonus. That is, the muscular coat of the vessel walls shows the same behavior as unstriped muscle elsewhere. This explains the superiority of rhythmic perfusion under the action of vasoconstrictor drugs, which superiority depends upon the increased elasticity and cannot be used to support the idea of an active participation of the blood-vessels in the passage of the blood.

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(1a—329½)

### An Analysis of the Nervous Control of the Cardiovascular Changes during Occlusion of the Head Arteries in Cats.

Cora Sennar Winkin, *Am. J. Physiol.*, 60:1, March 1, 1922.

It was desired to study the cardiovascular relations found in the mammalian organism under extreme conditions of stress. Occlusion of the head arteries gave a complete anemia of the brain, thus proving (Sec. 1—Page 824)

ducing a profound change in the internal environment of the animal. The experiments were carried out on cats to which ether was administered through a tracheal cannula. The head arteries were secured outside the thoracic wall, the branches of the left subclavian, separately secured in the axilla, the right carotid and right subclavian from within the carotid sheath in the neck; the left carotid held the blood pressure cannula. All the arteries were kept under ligatures ready to be occluded by clamps at the convenience of the experimenter. Prior to occlusion, ether was reduced until various obvious tests of the activity of the brain stem could be secured, the return of a vigorous corneal reflex always being awaited before the circulatory arrest was made. With the elicitation of the corneal reflex artificial respiration was begun, and the clamps on the arteries immediately adjusted. With the adjustment of the clamps, the entire series of peripheral effects follows; the eye reflexes are immediately lost, and within twenty seconds the more marked peripheral effects are released. Deep and labored breathing sets in, skeletal convulsions appear and a sharp rise of blood pressure is recorded (often reaching 200 mm. Hg or more). This, it was found, frequently outlasts the other functions; the pressure may not begin to fall until from ten to eighty seconds after respiratory failure. The time from the shutting off of the arteries to the circulatory failure was assumed as the complete occlusion time and was found to be about three minutes. Immediately after the reestablishment of the circulation there occurs a profound depression of all functions. Blood pressure continues falling markedly when the arteries are released, and finally reaches a level of about 50 mm. No other medullary responses are elicitable at this time. Artificial respiration was maintained throughout the period of depression and until such time as the bulbar functions again became evident. It was observed that if no further lesions are inflicted, occlusions of three or four minutes are usually followed by a beginning of recovery within seven minutes after release of the arteries. Eventually normal pressure is regained and the animal breathes quietly and regularly. About ten minutes after release of the arteries, pressure is usually normal, vibrissae are erect, and the corneal reflex is elicitable. At this point, a renewed occlusion of the head arteries may be done and the entire cycle repeated.

The author then investigated the following points: The rôle of the splanchnic constrictor fibers in the rise of pressure during cerebral anemia; the effect of bilateral vagotomy; the effect of excision of the stellate ganglions; the effect of excision of the entire cardiac innervation; the effect of the cardiac innervation on the anemic rise; the influence of the splanchnic nerves on the anemic rise; the relation of the adrenal glands to the rise of pressure during cerebral anemia; the effect of repeated occlusion on intact cats; the effect of repeated occlusions in cats deprived of adrenal glands; survival after adrenal ligation; and finally the relation of the splanchnic sympathetic system to the central nervous system as regards (a) a comparison of splanchnic response with other peripheral responses, and (b) the anatomic relations of the splanchnic outflow in its bearing on recovery after section of the spinal cord. The tabulated results show that the nerves of the heart are not essential either for the activation or for the persistence of the characteristic pressor phenomena of the anemic rise. In the early stages of cerebral occlusion the cardiac innervation

functions as a check on the rapid rise of blood pressure. In this moderating action, accelerators as well as vagi are involved, since on excision of the stellate ganglions, the vagi alone are unable to prevent an abrupt and steep rise of pressure. The activation and maintenance of the vascular responses under cerebral occlusion are controlled essentially by the splanchnic nerves. Differential section in various regions of the splanchnic outflow influences the level of the arterial blood pressure. The extent to which the pressure falls on section is an approximate index of the degree to which the anemic rise will be compromised by the lesion. It is impossible to influence the vascular response to anemia by indiscriminate sections within the splanchnic outflow. In order definitely to abolish the response, it is necessary to section either sufficiently far out in the periphery, or sufficiently high up in the spinal cord to interrupt completely the continuity between the medulla and the celiac ganglion. Cerebral occlusion, carried out in repeated succession, was borne as many as 18 times in intact animals. The occlusion time was in no way curtailed and the anemic increment of blood pressure only slightly diminished. The continued maintenance of blood pressure at an extremely high level, characteristic of the anemic rise, was not possible after gross interference with the supply of some product of adrenal activity. An increased liberation of adrenalin under extreme splanchnic stimulation could not be demonstrated as necessary for the characteristic contour of the anemic rise. This is apparently dependent on the amount of circulating adrenalin. An increased availability of some product of adrenal activity appeared demonstrable in intact animals under extreme splanchnic stimulation, after 8 or 10 successive occlusions had been inflicted. Survival after ligation of the adrenal glands could be reduced to one or two hours when the animal was subjected to successive repeated cerebral occlusions. A complete failure of vasomotor tone seemed demonstrable in these animals.

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**The Efflux of Blood from the Carotid Artery of the Dog and Its Expression by a General Empirical Formula.**

*Halbert L. Dunn, Arch. Int. Med., 29:368, March, 1922.*

In the numerous and extensive studies of blood pressure no attempt has been reported to establish a correlation between it and the blood flow. Such an attempt is here made. By means of quantitative methods and graphic analysis of results, a relationship between the arterial blood pressure and the efflux of the blood from a cannula, of known size, was obtained in experiments on dogs. Application of this relationship to direct arteriovenous transfusion can be made only after further observations carried out with human material. As to accuracy of the data, the cross section area of the lumen of the cannula can be determined with considerable exactness; the blood flow per ten seconds is also an accurate measurement. The blood pressure, however, is not an exact observation. The necessity for an absolutely accurate base line was not obvious while the experiments were being conducted. The error in its determination gave variations ranging from 2 to 10 mm. Hg. The efflux of blood reached a maximum average of 75 c. c. per ten seconds when a cannula of 9.512 sq. mm. in area was used. The relationship of the blood pressure, the efflux of blood from the carotid artery

of a dog, and the lumen of a cannula the cross section area of which ranges from 1 to 10 sq. mm., can be expressed by the general empirical formula: Blood flow (c.c.) =  $0.17 \times$  area (sq. mm.)  $\times$  blood pressure (mm. Hg.). The significance of this relationship between the flow of blood and the lumen of a cannula is not satisfactorily explained. Although the formula is definitely influenced by the size of the cannula a point is reached at which the size of cannula makes little difference in the amount of blood flowing from the artery.

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**The Effect of Carbonated Baths in a Healthy Person, with Remarks on the Influence of Altitude.**

*G. Liljestrand and R. Magnus, Pflüger's Archiv. f. d. ges. Physiol., 193:527, Berlin, Feb. 22, 1922.*

Experiments were carried out with cool carbon dioxide baths to test the chemical heat regulation (a regulation in response to cooling, not depending on muscular action) which Freund and his collaborators claim to have established on a basis of rabbit experimentation. Although the bather gives off considerable amounts of heat to the surrounding medium, he experiences in such baths a subjective feeling of warmth, due to the dilation of cutaneous vessels. Muscular tremor does not occur; thus physical heat regulation through the skin, and chemical heat regulation by muscular movements are ruled out. The experiments were carried on at St. Moritz, between July 10 and August 10, during the early morning hours, before breakfast. The bather was kept in a state of complete muscular quiet. Temperature of the water was 33° C. and it contained 680-730 c. c. CO<sub>2</sub> which was reduced about 10% during the three quarters of an hour consumed in the bath. Baths at 33° C. produce a definite sensation of warmth and a reddening of the skin, which appears in from twenty seconds to five minutes. Baths at 29° C. produce a definite local chilling; large gas bubbles form; at the same time there is a sensation of warmth in other parts.

The standard of comparison had previously been determined accurately for a test case. No increase in oxygen metabolism was observed in cool carbonated baths. In contrast to this constant factor is the increase in total ventilation, in consequence of which there is an increased CO<sub>2</sub> elimination, manifesting itself in a heightened respiratory quotient. The tests on this subject showed that under normal conditions the oxygen intake in the mountains (3000 ft.) is the same as in the low land, provided a sufficiently long preliminary period had removed the influences of the preceding day (muscular activity, sun's rays, wind). The ventilation per minute, calculated for 0° C. and 760 mm. Hg., showed a slight decrease from that obtained at Stockholm. When calculated for the existing barometric pressure, 37° for an atmosphere saturated with moisture, it was the same for both places. The increased elimination of CO<sub>2</sub> cannot be attributed to CO<sub>2</sub> absorption by the skin or to an increased production of CO<sub>2</sub>, but is, for the most part, the result of excess ventilation. This is apparent from the diminished alveolar CO<sub>2</sub> tension. In the carbonated bath the marked hyperemia of the skin causes an increased amount of heat to be given off, to which the distinct sensation of warmth corresponds. Since there is no increase in oxygen consumption, a lowering of body temperature must follow the

increased giving off of heat; this regularly occurs in the absence of any muscular activity. The dilation of the cutaneous vessels is due to the chemical effect of  $\text{CO}_2$ . There is a lowering of temperature even after preliminary muscle work. Presumably  $\text{CO}_2$  is one of the most effective agents for reducing temperature in healthy subjects. This probably explains the refreshing action of such baths, since there is no stimulation of metabolism. The warming of the skin prevents the appearance of muscle tremor, but it may occur after the bath and will be followed by immediate rise in temperature. The dilatation of the cutaneous blood-vessels permits an increased volume of blood to pass through the skin, and the minute-volume of the heart is definitely increased (in 4 cases the increase averaged 52%); at times it may remain unchanged, owing to compensatory contraction in other vascular areas. The pulse rate falls in accordance with the body temperature, and the volume increases. No marked alteration of blood pressure occurs. While these tests do not rule out a chemical heat regulation, it is certain that none is produced or influenced by cool carbonated baths.

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**The Rôle of the Sodium and the Carbonate Ions and of the Change in the Sodium-Calcium Ratio in the Contraction of the Isolated Duodenal Segment of the Albino Rat.**

*F. S. Hammett and J. E. Nowrey, Jr., Am. J. Physiol., 60:48, March 1, 1922.*

Previous studies have shown that the isolated duodenal segment of the adult male unexcited albino rat when suspended in oxygenated Tyrode's solution at body temperature contracts when small amounts (0.1 to 0.4 c. c.) of tenth molecular sodium carbonate solution are added to the surrounding liquid. Using the experimental procedure described previously, the authors found that this contraction is due neither to the increase in the sodium ions, nor in the sodium-calcium ratio, nor in the carbonate ions. The increase in the sodium ions may participate in the effect by increasing the permeability of the tissue for the agent initiating the reaction, but this increase in permeability can not be considered as the primary cause of the contraction.

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**The Rôle of the Change in Hydrogen-Ion Concentration in the Motor Activities of the Small Intestine.**

*Frederick S. Hammett, Am. J. Physiol., 60:52, March 1, 1922.*

In order to determine whether or not the observed contraction of the isolated intestinal segment of the albino rat was due to the increase in hydroxyl-ion concentration of the Tyrode's solution on the addition of tenth molecular sodium carbonate, a solution of sodium hydroxid was prepared which would give the same hydroxyl-ion concentration when added in the same amount to equal quantities (4 c. c.) of Tyrode's solution. By the indicator method it was found that the addition of 0.2 c. c. of a solution of sodium hydroxid of approximately twentieth molecular concentration to 4 c. c. of Tyrode's solution gave pH 9.4 to 9.8. The addition of 0.2 c. c. of a tenth molecular solution of sodium carbonate to 4 c. c. of Tyrode's solution gave the same pH. A

comparison of the two solutions in the Duboscq colorimeter showed satisfactory agreement in color depth. Intestinal segments were prepared and their responses to the addition of equal amounts of these solutions to equal amounts of Tyrode's solution in which they were suspended were recorded as usual. It was found that practically the same degree of contraction was obtained with the sodium hydroxid solution as with the sodium carbonate solution. This allows of no other conclusion than that the stimulus to contraction is the increase in the hydroxyl-ion concentration of the liquid in which the segment is suspended.

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**Action of Some Alimentary Substances on the Activity of Ptyalin in Acid Medium.**

*D. Maestrini, Morgagni, 64:102, Milan, Feb. 28, 1922.*

In a series of investigations the author tried to establish the resistance of human ptyalin to the action of HCl in an acid medium. The conclusions were as follows: (1) Starch paste (3-5%) in an acid medium affords to ptyalin a potent protection. (2) The protective effect is directly proportional to the concentration of starch and inversely proportional to the concentration of HCl and to the duration of contact of the acid with the enzyme. (3) Tolerably high concentrations of HCl, as they are present in the gastric contents of normal men, are not able to destroy, in the presence of starch, the amylolytic activity of human saliva. (4) Ptyalin which had remained in contact with HCl for three hours can entirely recover its enzymatic power after neutralization. (5) The maximal concentration of acid, tolerated by mixed human saliva, during a contact of six hours with HCl, is about 1.4 gm. per hundred; under action of higher concentrations the amylolitic power is not recovered, or only to a minimal degree. In a second series of experiments, the author studied the various alimentary substances to find whether that quality, protection of ptyalin, was specific for starch or whether it was also possessed by common protein substances and by fats. The conclusions were: (1) Egg albumin, diluted with distilled water, and ovoglobulin, afford to ptyalin a feeble protection against HCl. (2) Egg albumin diluted with physiologic NaCl solution, ovalbumin, blood-fibrin, oil of sweet almonds and mutton fat cannot protect ptyalin against HCl. To solve the second problem, investigation was made of the action upon ptyalin, in an acid medium, of very fine powder of animal charcoal. It was found that powdered animal charcoal has a protective action of ptyalin against HCl, and that this action is more marked than that of starch.

In order to explain the mechanism of this action, experiments were made to investigate whether and to what degree the various substances could fix enzyme. It had been observed that (1) pure commercial starch (either in powder, or as paste) can fix a large amount of ptyalin; this fixation is not very stable, because the enzyme can be taken away gradually, almost entirely; (2) oil of sweet almonds, fibrin of ox blood and mutton-fat cannot fix even minimal quantities of ptyalin; (3) Powdered animal charcoal fixes a large amount of ptyalin, even more than starch, but always in a rather unstable manner, so that ptyalin can be washed away. On the whole these experiments have proved (1) the powerful action of starch on human ptyalin against even high concentrations of

HCl, as they are found during digestion in gastric contents of normal man; (2) the absolute absence of that protective action in common alimentary substances, except when some of these (for instance egg albumin) are placed in special experimental conditions, which, however, are never encountered in ordinary life; (3) the powerful protective action afforded by substances of which even a small volume presents a large reactive surface (e. g., powdered animal charcoal).

These data indicate that ptyalin is not destroyed in the stomach, and after arriving in the intestine, after neutralization by gastric juice and bile, it may coöperate in the splitting of polysaccharids.

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**The Function of the Digestive Glands in Avitaminoses.**

*Koichi Miyadere, Biochem. Ztschr., 124:244, Berlin, Nov. 21, 1921.*

As it is claimed that the disturbances in the course of vitamin-free feeding are due to deficient function of the digestive glands thereby causing poor utilization of the food, the behavior of the gastric secretion on a vitamin-free diet was investigated. The experiments were conducted on a dog according to the Pawlow method. The diet consisted of polished rice and pure wheat albumin; during the last week the animal also received an addition of vitamin-free lard, in order to determine whether the gradual loss of weight can be inhibited by the addition of such fat. Secretory tests were made both previous to the administration of the vitamin-free diet and during its course. Vitamin-free butter and alcohol were also added to the test diet, the alcohol because it is a secretory stimulant.

The experiment showed that almost no gastric juice was formed with the rice and wheat albumin diet, but on addition of alcohol, the stomach responded with marked secretion. This proves that the power of secretion of the gastric glands is not disturbed in avitaminosis, but that in selected vitamin-free diet mixtures, all stimulating substances were absent. It is therefore not the lack of vitamin but the absence in the usual vitamin-free food mixtures of the substances stimulating secretion which causes the disturbance. The gastric secretion continuously diminished on the rice diet because the dog ate it with increasing aversion, the longer the experiment lasted. The increased secretion after alcohol might be attributed to an injury of inhibitory nerve fibers; in fact, anatomic changes in the vagus and in other nerves have been demonstrated in beriberi.

(1a—333½)

**Variations in Output of Bile Salts and Pigments during Twenty-Four Hour Periods. Observations on Standard Bile Fistula Dogs.**

*F. P. Wisner and G. H. Whipple, Am. J. Physiol., 60:119, March 1, 1922.*

Several 24-hour collections were made on standard bile fistula dogs, following the method as the operative procedure and general hygienic routine. The weekly routine consisted of a single 6-hour collection on the first four days of the week, followed by 4 consecutive 6-hour collections on the fifth day. The specimens of bile secured were analyzed for their content of bile acids and bile pigments. Bile

fistula dogs show little if any difference in the output of bile, bile-salts or bile-pigments during 4 consecutive 6-hour periods. Complete dissociation of the bile constituents could be demonstrated after a large dose of taurocholic acid. Following a 2 gm. dose, a great rise in bile salt content was observed during the first 6-hour period. During the second 6-hour period the bile salt content was about normal but the cholagogue action was still in evidence and the fluid output therefore was dissociated from the bile salts. The bile-pigments were constant before and after the period of bile salt administration.

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**Organic Foods with Specific Action. XI. Experiments on Pigeons.**

*Emil Abderhalden, Pflüger's Arch. f. d. ges. Physiol., 193:329, Berlin, Feb. 9, 1922.*

If hungering pigeons be given that small amount of dried yeast (0.5 gm.) which is capable of protecting the animals against alimentary dystrophy when fed exclusively on polished rice, the drop in body weight is more rapid than under complete deprivation of food. This is obviously the expression of increased cellular metabolism. Heating the dried yeast one hour at 120° C. destroys the accelerating action on metabolism and on loss of weight. Rice extracted with hydrochloric acid leads to rapid loss of weight. Yeast pills cause a rise of the falling temperature though body weight continues to decrease. The cause of the drop in weight is loss of nutrient value of the rice on the one hand and withdrawal of nutramins on the other. Only the latter are supplied by yeast. Dried yeast dating back to 1903 was still thoroughly efficacious. The same action is possessed by yeast autolysate which well stands drying at low temperatures. Extraction of yeast with water, chloroform and acetone by no means removes the active principles completely. Bran is as efficacious as yeast. The brain substance of normal pigeons possesses activity, though much less than that of yeast and bran, while brain substance taken from pigeons that had just succumbed to alimentary dystrophy was found wholly inactive. The addition of fructose-sodium diphosphate and potassium phosphate, or of formic acid, oxyisobutyric acid and oxybutyric acid was unsuccessful. This action of the yeast is, therefore, due not to known but to unknown substances that are sensitive to higher temperatures. Evidently nutramins are essential to cellular metabolism. Undoubtedly they are catalysts which accelerate metabolic processes and, above all, play a prominent part in oxidations. Whether they interfere actively herein, or bring about definite conditions essential to oxidations is as yet undecided. These substances apparently cannot be formed by the animal organism nor are they capable of being stored except in slight amounts. Nutramins are able to accelerate fermentative processes (alcoholic yeast fermentation) in an unknown manner so that comparison of the same supplies the means for investigating their action and for obtaining conceptions of their nature. The injuries caused by nutramin-deficient feeding are not to be designated by polyneuritis, as inflammatory or degenerative changes of the nervous system are absent. And the prompt action of injections of yeast or bran preparations in spasms in affected animals supports this view. It is better to speak of

alimentary dystrophy, whose phenomena are probably related to diminished possibility of oxidation of all cells. The direct transference of the observations made in rapidly growing animals (rats, birds) to other animals is not possible and vitamin feeding in man has yielded decided therapeutic success only in scorbutus. In any case great care is demanded in the conservation of food in order to guard against the destruction of the substances in question.

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**Organic Foods with Specific Action. XII. Comparative Researches on the Behavior of Weight Content of Single Organs in Pigeons Fed on a Normal Diet or on an Exclusive Diet of Polished Rice with or without Yeast and Those Starved Completely.**

*Emil Abderhalden, Pflüger's Arch. f. d. ges. Physiol., 193:355, Berlin, Feb. 9, 1922.*

The organs were removed immediately after death, weighed and dried at 110° C, water content being determined by subtraction. The greatest loss of weight occurs in striated musculature. In starving animals the stomach showed slight, and in animals suffering from alimentary dystrophy somewhat larger, loss of weight. The intestinal canal lost greatly in weight and its water content was increased thereby, but less in dystrophic than in starving animals. After feeding on polished rice with yeast the weight of stomach and intestine diminishes gradually while water content increases. The liver, and pancreas behave similarly, their water content being, however, little altered, the alterations being most marked in starving animals. No specific relationship of loss of weight and increased water content of organs could be determined in dystrophic animals as compared with those fed on polished rice and yeast. Both groups indicated that the condition is one of protracted hunger which obviously depends on inadequate assimilation of food owing to nutramin deficiency. To the hunger condition are added phenomena of alimentary dystrophy, namely, loss of appetite, restricted glandular activity, disturbance of gaseous exchange, lowering of body temperature, spasms and eventually paralysis. In pigeons that maintained their normal weight three or four months on a diet of polished rice with 0.5 gm. yeast, the weights of organs differed little from those of normal animals.

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**Vitamins. II. Acceleration of Fermentation by Extracts from Animal Organs.**

*Sigmund Fränkel and Josef Hager, Biochem, Ztschr., 126:189, Berlin, Feb. 15, 1922.*

The addition of extracts from animal and vegetable embryos in small amounts to a yeast fermentation accelerates strongly the latter. This activating capacity is also possessed by a series of salts of aliphatic fatty acids, ox acids, ketonic acids and dicarbonic acid, as well as by aldehyds. The activity of these substances either persists almost equally from beginning to end of the experiment, when they are termed permanent accelerators, or strong activity is shown only at the beginning

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of the experiment, decreasing during the course of fermentation. In the latter case they are termed initiators. From the animal organs water-soluble extracts were prepared which proved to be permanent accelerators. The method of preparation consisted in the purification of the animal organs from blood and adhering fat and subsequent exhaustive extraction with about 80% alcohol. The solution was concentrated at a low temperature in vacuo, shaken with ether to remove fat and concentrated to 50 c.c. on the water bath. The organic part of the extract was determined by incinerating the extract and calculating the organic extractive substances of the entire original material of the respective organ from the difference in weight before and after incineration. Into 2 azometers filled with mercury, 5 c.c. 10% yeast infusion and 10 c.c. 10% cane-sugar solution were drawn; 1 c.c. of the prepared extract solution was added to the one and 1 c.c. water to the other, so that the total volume was the same in both azometers.

The experiments were conducted at 28° C. and occupied three hours. In each extract experiment acceleration was denoted after a quarter of an hour by the increased production of carbonic acid, as against the control experiment. The researches were recorded by tables and curves. The tables show that all the extracts examined exhibited accelerating action though fluctuations in the degree of acceleration occur within the experimental period. An exception is formed by bone-marrow, whose behavior is quite indifferent toward alcoholic fermentation. Also, the anterior and posterior pituitary lobes do not produce satisfactorily appreciable acceleration on the addition of 1 c.c. extract solution. As the basis for determining comparative values 2 units were selected, namely, the extract unit of 0.1 gm. and the original material unit of 100 gm. On the basis of the observed total acceleration, that is, the difference between the volumes in the extract experiments and control experiments and the amount of extract from the respective organs producing the same, the degree of acceleration was determined for the different organs by bringing the total accelerating volume of the normal volume into relationship with the normal volume. From the foregoing proportionate values it appears that the sequence of the organs arranged in accordance with increasing extract unit values is by no means the same as for the values of original material units. Only the gray matter of the cerebellum, strange to say, shows a maximum in both cases.

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Vitamins. III. Fermentation Accelerating Plant Extracts and the Action of Cholin and Amino-Ethyl Alcohol on Fermentation.

Sigmund Fränkel and Albert Scharf, *Biochem. Ztschr.*, 126:227, Berlin, Feb. 15, 1922.

As beriberi and scurvy symptoms disappear after consumption of fresh vegetables, the latter were examined by the method devised by the authors several years ago. Mattei's researches seemed to show the value of an extract from roasted coffee in polyneuritis, while one from unroasted coffee was inactive, so that both these extracts were likewise investigated. The vegetables were finely comminuted in the fresh state and extracted with 80% alcohol. Legumes and coffee were pulverized in a mill. The preparation of the extracts and the quantitative estima-

tion were carried out by Fränkel and Hager's method: In order to obtain a standard for ferment acceleration 100 gm. yeast were extracted with alcohol, and the standard so obtained was used as a basis for comparison. Most catalyzers fell below this standard; only a few exceeded the activity of yeast extract. In white flour the amount of catalytic substance, or vitamin, was minimal; dark flour contained larger though not very large amounts. Polished rice showed no ferment acceleration. Beans, kale, cabbage and spinach accelerated fairly strongly. Carrots, on the other hand, showed less catalysis as the yellow pigment is not related to the activity of the substance. The great activity of kale and cabbage in fermentation coincide with the results of animal experiments. Little activity was displayed by hulled peas and lentils which points to the localization of vitamins in the hulls. Yellow maize likewise had little activity, and in this case also the yellow pigment is of no moment. Corn-bran, egg-yolk extract and potatoes, which are excellent antiscorbutics, are moderately catalytic. Onion extract and turnip cabbage extract are very active. Legumes and roots have a weak, and leaf vegetables a strong action. Very great activity is manifested by the leeks. Egg-yolk possesses great and celery the greatest catalytic power. Unroasted coffee was inactive, but roasted coffee was quite active; obviously a vitamin or similar substance is formed during the roasting. Caffein itself is inactive. As cholin (which retards), was found in the extract, the latter was also examined for the second base of the unsaturated phosphatids—cholamin (beta-amino-ethyl alcohol).

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**Vitamins. IV. Experiments on the Adsorption of Vitamins.**

*Sigmund Fränkel and Albert Scharf, Biochem. Ztschr., 126:265, Berlin, Feb. 15, 1922.*

According to Michaelis and Ehrenreich, enzymes are adsorbed differently by different clays. Acid enzymes are adsorbed by aluminum hydrate and basic ones by acid clays like fuller's earth or kaolin. In this way the separation of different enzymes was attempted. The adsorption capacity of fuller's earth, kaolin and aluminum hydrate for vitamin was therefore investigated, for which purpose an alcoholic yeast extract purified with ether was employed after the purification with lead and mercury. The mercurial precipitate was decomposed, hydrochloric acid removed and 1 c.c. of the liquid utilized for accelerating fermentation. Equal amounts of the liquid and the respective adsorption agent were then shaken, allowed to stand over night, filtered, washed with cold water and the acceleration of fermentation of the filtrate, which was previously brought up to the same volume in vacuo, was examined. Total or partial adsorption of the substance could then be determined from the reduction of acceleration. It appeared that fuller's earth adsorbs most of the substance, that kaolin adsorbs it entirely and while aluminum hydrate is inactive. The vitamin is, therefore, basic as is proved also by the chemical method of preparation.

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Vitamins. V. Further Experiments on the Chemistry of Vitamins.

*Sigmund Fränkel and Albert Scharf, Biochem. Ztschr., 126:269, Berlin, Feb. 15, 1922.*

The isolation of the vitamin by corrosive sublimate without loss from the aqueous solution of the alcoholic extract that had been previously purified with lead and freed from fat, was investigated comparatively in rice-bran extract and yeast extract. A considerable quantity of rice-bran extract was dissolved in water, digested with basic lead acetate, allowed to stand one day and filtered. Lead in the filtrate was removed with sulphurated hydrogen and the filtrate freed from the latter with carbonic acid. The vitamin solution was digested with concentrated alcoholic sublimate solution, allowed to stand several days in the dark and filtered. From the filtrate mercury was removed with sulphurated hydrogen, hydrochloric acid neutralized by lead carbonate, and lead again precipitated with sulphurated hydrogen. The sulphurated hydrogen was again removed with carbonic acid, the neutral liquid causing under test strong retardation of yeast fermentation. Therefore, there was present in the extract a nonprecipitable retarding substance besides the accelerating substance precipitable by mercury. The mercury chlorid precipitate was suspended in water, treated with sulphurated hydrogen, carefully washed and purified with lead carbonate as before. The filtrate, having been finally freed from sulphurated hydrogen, was rendered alkaline by sodium bicarbonate shaken with amyl alcohol and the base then removed from the amyl alcoholic solution with 1% HCl. Both the amyl alcoholic solution and the aqueous hydrochloric solution contained a carbohydrate which reduced Fehling's solution only after boiling with dilute acid. The alcoholic filtrate was digested with excess of alcoholic platinum chlorid solution, allowed to stand overnight and the crystalline precipitate recrystallized from very little water. Analysis of the platinum salt disclosed the presence of cholin. Suzuki maintained that the antineuritic substance is a combination of cholin, grape-sugar and nicotinic acid.

Experiments show that after removal of the greater part of the inactive substance, cholin is still present in the final extract not in chemical combination but in the free state. Owing to lack of material the experiments were conducted with yeast, 3 kg. pressed yeast being employed. After drying, the latter was extracted with alcohol, boiled several times with water, concentrated in vacuo, again treated with alcohol and fat removed with ether. Finally the liquid was precipitated with basic lead acetate and the filtrate freed from lead by sulphurated hydrogen. The solution concentrated in vacuo was precipitated with concentrated alcoholic sublimate solution. Precipitate and filtrate were purified in the manner previously described and the precipitate, which was for the most part inorganic, did not accelerate fermentation while the solution, after careful evaporation of the alcohol in vacuo, produced acceleration. On treating the solution with platinum chorid, cholin was again found. Cholin therefore appeared in the company of the vitamin in rice-bran as well as in yeast. Micro-analysis by Progl's method gave nitrogen 4.75% of the mercurial precipitate. The substance did not give Molish's carbohydrate reaction and the assumption of a glucosic structure of the vitamin must therefore be abandoned.

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**Further Observations on the Distribution of Vitamin B in Some Vegetable Foods.**

*Thomas B. Osborne and Lafayette B. Mendel, J. A. M. A., 78: 1121, April 15, 1922.*

These experiments supplement earlier ones conducted by the same technic, and indicate that asparagus, celery, dandelion, lettuce and parsley all contain noteworthy amounts of vitamin B. The tests were made on young white rats, weighing 40-80 gm., which were failing to grow at the age of about 50 days on a diet demonstrated to be adequate to bring increment in body weight at a normal rate when sufficient vitamin B was supplied. The food mixture consisted of casein, 18%; salt mixture, 4%; starch, 54%; butter fat, 9%; lard, 15%. Feeding of from 100 to 200 mg. dried brewery yeast daily in addition to this ration suffices to induce adequate food intake and growth at a normal rate for young rats. Asparagus proved to be unexpectedly rich in vitamin B. With dandelion leaves and parsley the results were not so good. If these vegetables are considered with respect to their content of vitamin B in comparison with apples and pears, or the juice of grapes, then asparagus, celery and lettuce, at least, will be found to exhibit a larger vitamin B potency in terms of the edible product consumed. This evidence gives added justification for the nutritive prominence of the vegetable products examined, and serves in part to emphasize their importance in the diet of man.

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**Some Plant Sources of Vitamins B and C.**

*Francisco O. Santos, Am. J. Physiol., 59:310, Feb. 1, 1922.*

A series of studies was made on the vitamin content of the fruits and vegetables eaten by the Filipinos. Such plant foods as togi, okra and avocado were found to be comparatively high in vitamin B. One-half gram of each of these as daily supplement to the standard vitamin-B-free diet caused the recovery in weight of rats which had been declining because of this accessory food factor. Mongo, sweet potato leaves and duhat were found to contain enough vitamin so that 1 gm. of them as daily supplement caused the recovery in weight of rats which had been declining for lack of vitamin B. Artichokes, bilimbi, banana flower bud and bamboo shoots were found to be relatively poor in vitamin B, and mongo poor in vitamin C. The vitamin B in mongo was found to be increased in germination. Togi when fresh is relatively rich in vitamin C, but after it is prepared for culinary use, the latter is destroyed. Santos verified, in the case of mongo, the observation of several investigators that vitamin C is increased when peas, lentils and beans are germinated. Ten grams of mongo as daily supplement to the scorbutic diet failed to protect guinea-pigs from scurvy, while 5 gm. fresh togi as supplement to the same scorbutic diet cured 3 guinea-pigs of the disease.

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**Water-Soluble B and Bios in Yeast Growth.**

*Ellis I. Fulmer and Victor E. Nelson, J. Biol. Chem., 51:77, March, 1922.*

In order to check previous data, the following experiment was  
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made: Dried alfalfa was extracted for twelve hours in a continuous extractor with 95% alcohol. Varying concentrations of the extract were added to Medium F which had the following composition: 100 c.c. contained 0.188 gm. of ammonium chlorid, 0.100 gm. of calcium chlorid, 0.100 gm. of disporassium phosphate, 0.04 gm. of precipitated calcium carbonate, 0.60 gm. of dextrin, and 10 gm. of cane-sugar. The flasks were inoculated with an initial count (when the count equals 1 there are 250,000 cells per c.c.) of about 4, the yeast being taken from cultures which had been growing in Medium F for two years. The cultures were incubated at 30° C. After forty-eight hours, the yeast count was determined, and the results tabulated. It was found that the addition of alcoholic extract of alfalfa did not improve Medium F, thus verifying a previous statement that not only is water-soluble B not necessary for the growth of yeast but also it is of no advantage in Medium F.

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**A Reply to Fulmer, Nelson, and Sherwood Concerning Medium F.**

*Walter H. Eddy, H. L. Heft and H. C. Stevenson, J. Biol. Chem., 51:83, March, 1922.*

This paper is intended as a comment upon the preceding article. The authors prepared an alcohol extract of alfalfa after the manner of Fulmer and his associates and used this in the concentrations given by those authors and in higher concentrations. In their incubations the present authors set their incubator at exactly 30° C. The Funk method of measurement of total growth was used, and the results tabulated. Eddy, Heft, and Stevenson remark that the results obtained make them sceptical as to the qualitative differences in alcohol and water extract, since they again secured stimulation of Medium F and with the alcohol extract. The stimulation is not so great as with the water extract, which is in harmony with the view that they had held, that alcohol is a poorer extractant of vitamin B than is water. The results obtained which showed greatest stimulation were with concentrations much greater than those used by Fulmer and associates. These facts combined with what the authors believe to be greater accuracy in their measuring, might, they believe, account for the failure of Fulmer and associates to observe stimulation with the alcohol extract.

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**Fat-Soluble Vitamin. X. Further Observation on the Occurrence of the Fat-Soluble Vitamin with Yellow Plant Pigments.**

*H. Steenbock and Mariana T. Sell, J. Biol. Chem., 51:63, March, 1922.*

A demonstration of fat-soluble vitamin activity was made with rats taken at an age of three to four and one-half weeks and put on a basal ration of salts, casein, dextrinized starch, and a source of water-soluble vitamin, with which the unknown to be tested was incorporated. The salts used were respectively Salt Mixture 32, the composition of which one of the authors has given in a previous communication, and Salt Mixture 38 which represented a mixture of 3 parts of Salt Mixture (Sec. 1—Page 837)

32 with 1 part of Salt Mixture 35. The casein was a high grade of commercial casein purified by daily washings for a week with dilute acetic acid. The dextrinized starch was prepared by barely moistening cornstarch with a 0.1% solution of citric acid and then autoclaving it for three hours at 15 lbs. steam pressure. After drying for at least a week it was ground to a fine powder. The water-soluble vitamin was incorporated with different materials. In some of the experiments the authors used 40% of white corn. In some instances 2% of dried yeast was used as the carrier of the water-soluble vitamin and again in other cases 3% of ether-extracted wheat embryo or a larger amount of the alcohol extract of ether-extracted wheat embryo evaporated on and made up to the original weight of the wheat embryo. The sweet potatoes were sliced and dried at room temperature in an air current. The carrots were trimmed to remove the crown in order to avoid contamination of the root with the attached leaf stems. They were shredded in a power-mill and dried at room temperature in an air current. From the tabulated results one learns that the fat-soluble vitamin often occurs most prominently where there are found the largest amounts of certain yellow pigments. White sweet potatoes and white carrots were found to contain little fat-soluble vitamin which stands in marked contrast to the authors' observations on the yellow pigmented varieties. The tops of white carrot roots, slightly pigmented with chlorophyll and containing a small amount of yellow pigment were found richer in fat-soluble vitamin than the bottoms containing only one-half as much pigment. Green cabbage leaves taken from the heart of cabbage plants which failed to head were found much richer in fat-soluble vitamin than white cabbage leaves in the head. The latter contained only one-tenth as much yellow pigment. The charts in the article show the growth curves of the rats on the various diet mixtures. The tabulated data show the results of the biweekly weighings of each rat while on the various diets, as well as the general condition of the animals.

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**Chemical Factors in Nutrition.**

*L. Mendel, Bull. Soc. scient. d'hyg. aliment., 9:587, Paris, Dec. 1921.*

Nutritive units present in the blood are comparatively simple compounds. They are used either for oxidation or for tissue building. Amino-acids, purins, nucleosids, simple sugars and fats constitute typical examples of such substances, which may be used as indicated above, or stored. Some organisms, such as yeasts, require relatively simple food and small variety. The food of other organisms may be more complex. Plants synthesize abundantly, animals relatively little. Proteins contain 18 or more amino-acids, or building stones. These compounds are obtainable from a wide variety of proteins including milk, eggs, meat, grains and vegetables. Nutrition is not only a question of providing, but of utilizing, food materials. In diabetes, glucose cannot be burned. Diabetes and obesity are closely related. Accessory substances, or vitamins, are necessary, but are present in a mixture of ordinary foods. The tendency to allow pharmaceutical products to replace food is unfortunate. It is dangerous to abandon a varied, sufficient and habitual diet. This principle is illustrated in beri-

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beri, scorbutus, and other diseases referable to defective nutrition. Food problems were not well solved by the different nations during the war.

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Experiments Developing Technic for the Study of the Chemistry of Nutrition and Growth.

*J. F. McClendon and W. S. Bowers, Minnesota Med., 5:203, April, 1922.*

Rats were placed on the following diets: (a) raw lean beef; (b) cooked lean beef; (c) oats with 1 gm. raw lean beef a day; (d) oats with 1 gm. cooked lean beef a day; (e) oats and corn meal, (f) oats and soy beans; (g) spinach, wheat flour and milk powder. At the end of three months x-ray showed that the bones in (g) were heavier and cast deeper shadows than the bones of the rest of the series. In a second experiment, 7 rats were fed a basic diet of equal parts of soy bean flour, oat meal, rye flour, and corn meal, plus 4 times this amount of wheat flour, and in addition different quantities of milk powder. The rat without milk powder died. The other rats grew in proportion to the percentage of milk in the diet. After a while, however, all those with the higher percentages of milk grew to normal adult rats, and it was only with the lowest percentages of the milk that a difference in growth appeared. In the third experiment oats were fed ad libitum, and an accurately measured amount of reconstituted milk powder a day was given each rat. All the rats had growth curves below normal, more marked in those receiving less milk. Calcium determinations on the bones showed practically no difference, but all had a diminished calcium content. In the fourth experiment, 10 rats were fed on a basic diet of 10% pure casein, 6% sea salt, and 84% wheat flour. Control experiments showed that this mixture was adequate in protein, in the total calories and in inorganic salts; it had perhaps half the required quantity of vitamin B, but no vitamin A. To this basic diet was added, in different percentages, powdered spinach. At first these rats grew in proportion to the spinach up to 5% spinach, but those on 6 to 9% did not grow faster than the one on 5%. After they had attained 100 gm. in weight, the ones on 4% and 5% spinach grew no faster than the one on 3% spinach. The one on 0% spinach developed ophthalmia and died. In experiment (5) 8 rats were placed on a diet of pure casein 12%, white flour 60%, pure cane sugar 20%, dried yeast 3%, sodium chlorid 2.5% and calcium oxid 2.5%. They also received cod-liver oil 0, 2, 3, 4, 5, 6, 7 and 8 drops, respectively per week. Calcium determinations on the tibia of these animals showed a diminished amount of calcium in the bones, being most marked in those that received only small amounts of cod-liver oil. Growth curves were all below normal. In experiment (6), a litter of six rats received 70% white flour, 20% sugar, 3% dried yeast, 2% milk powder, 2.5% sodium chlorid, and 2.5% calcium oxid. Growth curves were all below normal. At the termination of this experiment, the animals were divided into 2 groups and for five days were given a calcium-free diet, consisting of hydrogenated fat, sugar, calcium-free filter paper and sodium chlorid. In addition, the second group of rats received calcium-free butter fat. The calcium output in the excreta of group 1 (3 rats) was 11 mg., in

group 2 (3 rats) was 10 mg. This may have indicated a slightly greater retention of calcium in the bones of the rats receiving butter fat, which contains vitamin A. Experiment (7) was made to determine the antiscorbutic action of concentrated orange juice. The guinea-pigs receiving no orange juice died of scurvy in three weeks. The three receiving the least amount lost weight and developed typical scurvy in about 20 days. The other guinea-pigs, receiving a large amount of orange juice, gained steadily, the growth being proportional more or less to the amount of orange juice. In experiment (8), the concentrated orange juice was diluted with distilled water, then treated with Fuller's earth containing enough calcium carbonate to precipitate the citric acid, filtered with the suction filter; the calcium was precipitated by adding potassium oxalate a few drops at a time and then centrifuging, the process being repeated until no further precipitate remained. Toluol was added as a preservative. This product was fed by means of a pipette to the extent of 4 c.c. a day to 3 guinea-pigs that had severe scurvy and were below their original weight. On this treatment they ceased to lose and steadily gained in weight up to the time of closing the experiment.

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**Reductions and Oxidations and a Coupling Reaction in the Intermediate Metabolism of the Animal Body.**

*F. Knoop, Biochem. Ztschr., 127:200, Berlin, Feb. 28, 1922.*

Animal and plant chemism differ only in respect to quantitative relations, but the physiologic processes are extremely complicated. If pigs are fattened on potatoes (fat being formed from carbohydrate) an aldol condensation of acetaldehyd or of pyroracemic acid molecules is the most probable form of such synthesis, which are then followed necessarily by extensive reductions of  $\text{CHOH}$  to  $\text{CH}_2$  groups. Reduction in the animal body certainly does not proceed as in the laboratory with nascent hydrogen, or by transference of the elementary gas by catalysts. Free hydrogen is not at all probable, nor is the animal body capable of utilizing sunlight directly for reduction, like the plant. Rather, the fixation of energy must be attended by oxidizing processes of at least equivalent thermal value. A paradigm is supplied by Cannizzaro's transposition which is widely distributed in the animal body, wherein two molecules of the same kind need not always be altered so that the one evolves as much energy under oxidation as is stored by the other. For instance, a carbonyl might be oxidized to carboxyl while, simultaneously, in another substance a double compound would be reduced. The unknown reagents were termed hydroclastic ferments, which are said to decompose water in such a manner that oxygen is believed to become active in one direction and hydrogen in the other.

For the examination of reductions, butyric acid and pyroracemic acid were employed. As compared with carbohydrates, amino-acids are certainly products of far-reaching oxidation, because none of the carbon atoms, except carboxyl groups, contains oxygen, which is contained in all carbon atoms of sugar molecules. One method of synthesis adopted by the animal body is that over a-ketonic acid. This is evidently a reduction process which is attended by the elimination of one oxygen atom. In one case it was found that the amino-acid formed

did not appear as such but in the form of an acetyl product. This observation, inasmuch as acetic acid is an oxidate of other molecules, raised the question whether oxidation and reduction could be shown to be governed by each other, because the reduction process and the accumulation of nitrogen were associated with the coupling of a third substance produced by oxidation. The acetic-acid component of such a coupling reaction would have to originate from the principal foods, namely albumin, fat and carbohydrates. In order to demonstrate this, dogs were given 0.5 kg. horseflesh with 6 gm. phenylaminobutyric acid, the acetyl product of the amino-acids being estimated quantitatively in the urine. The average for two days was 1.27 gm. Then this butyric acid was supplemented by 6 gm. pyroracemic acid, and in other dogs by 6 gm. butyric acid. In the first case 1.89 gm., and in the second case 1.5 gm., acetyl products were obtained. The percentage increase was therefore 48.8% with pyroracemic acid and 18.1% with butyric acid. Amino-acid becomes imino-acid, or oxyamino-acid, and reacts as such with pyroracemic acid, the two different molecules being disproportioned in such a manner that pyroracemic acid is oxidized to acetic acid, while imino-acid is again reduced to amino-acid, whereupon both molecules unite to form acetyl amino-acid.

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**The Influence of Putrefaction Products on Cellular Metabolism. II. On the Influence of Phenylacetic and Phenylpropionic Acids on the Distribution of Nitrogen in the Urine.**

*Yoshizumi Hijikata, J. Biol. Chem., 51:141, March, 1922.*

In these experiments a number of rabbits were maintained in N balance by feeding "tofukara," while others were fasted. The total nitrogen was determined by the Kjeldahl method, the urea by means of urease, the ammonia by the method of Kruger, Reich, and Schittenhelm, and the amino-acids by Van Slyke's method. In Experiment 1 a rabbit in N balance received 0.5 gm. phenylacetic acid mixed with his food, and on the following day, 1.0 gm. In both administrations the acid was neutralized with sodium carbonate solution. On both days the excretion of amino-acids increased strikingly, while that of the total nitrogen was unchanged, causing a considerable increase in the proportion of the former to the latter. The excretion of ammonia was unaltered. The fact that there was no increase in the total nitrogen excreted was to be expected, since the amount of acid administered was too small to cause any decomposition of tissue proteins. In Experiment 2 a rabbit in N balance received on two successive days, by means of the stomach tube, 1.2 gm. phenylacetic acid, dissolved in sodium carbonate solution. On both days, not only the output of amino-acids, but also those of total nitrogen, urea, and ammonia were increased, in spite of considerable interference with the appetite. While the relative quantity of urea was very slightly decreased, the relative quantities of ammonia and amino-acids were more than doubled. In Experiment 3 the rabbit received tofukara until fasting was begun; then 35 c.c. water once daily through the stomach tube. On the fourth and fifth days of fasting, it received 1.0 gm. of phenylacetic acid, neutralized with 35 c.c. sodium carbonate solution through the stomach tube. The total nitrogen excretion decreased during fasting until the acid was

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administered. There was then an increase for two days followed by decrease. The output of urea, ammonia, and amino-acids showed increase; the urea absolutely and the others both relatively and absolutely. In Experiment 4 the rabbit received the phenylacetic acid subcutaneously, the results agreeing with the preceding experiments in which the substance was administered perorally. In Experiment 5 a rabbit was maintained in N balance. It was given phenylpropionic acid during 2 periods of two days each. The acid was neutralized with sodium carbonate solution and introduced through the stomach tube. On Dec. 15 and 16 the animal received 1 gm. of the acid. On Dec. 21 and 22, 1.5 gm. was administered. The total nitrogen and the ammonia excreted were practically unchanged when the acid was introduced. The output of ammonia increased strikingly on both occasions, both absolutely and relatively. In the first case, urea decreased relatively and in the second both absolutely and relatively. The amino-acids were greatly increased. In Experiment 6 a rabbit in N balance, was treated in the same manner as the preceding one but with larger doses. On Dec. 23 and 24, it received 2.5 gm. daily of neutralized acid and on Dec. 28 and 29, 3.5 gm. daily. On the first day in which the acid was administered, the total nitrogen excreted was increased. On the second day, it was normal. There was, also, an absolute increase in the output of urea on the first day. Relatively, however, it was decreased on both days. Both absolutely and relatively the ammonia and amino-acid excretions were increased on both days on which acid was given. During the second period of feeding the acids, similar changes were observed but of greater degree. In Experiment 7 a rabbit was fed with tofukara for a time and then fasted. During the experiment it received 35 c.c. water daily. On the fifth and sixth days, 3.0 gm. of acid in 35 c.c. of sodium carbonate solution was introduced through the stomach tube. The total excretion of nitrogen decreased regularly until the acid was administered. It then increased, with the exception of the seventh day. The urea also rose absolutely, beginning with the fifth day, but on the two days in which the acid was given it decreased relatively. The ammonia excretion paralleled that of the total nitrogen. There was a great increase in the quantity of amino-acids both absolutely and relatively. In Experiment 8 a fasting rabbit received, on the fourth and fifth days, two subcutaneous injections of 1 gm. each of phenylpropionic acid in 20 c.c. of sodium carbonate solution. On both days the total nitrogen, as well as the urea and amino-acids, was increased. Relatively, however, the urea decreased. On the second day, the absolute quantity of ammonia was increased but there was relatively no change. The increase in the amino-acid excretion was both absolute and relative. Subcutaneous administration of phenylpropionic acid yielded the same results.

The experiments show that both substances under investigation have the same effect on the distribution of nitrogen in the urine.

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**Studies in Carbohydrate Metabolism. III. A Study of Urinary Sugar Excretion in 26 Individuals.**

*Isaac Neuwirth, J. Biol. Chem., 51:11, March, 1922.*

The author examined samples of twenty-four hour urine specimens voided by 26 subjects. The majority of the subjects were medical (Sec. 1—Page 842)

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students. All urines were preserved with toluene during their collection. They were analyzed for reducing substances both before and after fermentation. Dextrose was always used as a check on the activity of the yeast. In all cases, qualitative examinations of the urines were made for sugar, albumin, and indican by means of the Benedict, heat-acetic acid, and Obermayer's tests, respectively. Records were kept of the food taken by each subject in these experiments. The tabulated results show that the total sugar output for twenty-four hours varied from 614 to 1,383 mg.; the fermentable reducing substances varied from 134 to 488 mg.; the nonfermentable reducing substance varied from 370 to 1,024 mg. The nonfermentable sugar amounted to from 51 to 86% of the total sugar. The absolute percentage of sugar in the urine before fermentation varied from 0.037 to 0.208%; after fermentation, it varied from 0.027 to 0.112%.

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**The Rôle of Acid in Carbohydrate Metabolism. V. The Action of Acid and Alkali on Carbohydrate Metabolism in the Yeast-Cell.**

*H. Elias and St. Weiss, Biochem. Ztschr., 127:1, Berlin, Feb. 28, 1922.*

Small amounts of acid are capable of mobilizing glycogen from the liver. The action of acid on carbohydrate metabolism in liver-cells may be explained in three ways: (1) The acid in the splanchnic endings causes hyperirritability. (2) The action of the acid depends on activation of residual adrenalin in liver-cells. (3) A direct cellular action by the acid is involved. To decide this question experiments were carried out with acids and alkalies on cells that contained glycogen but had no nerve-endings and had not come in contact with adrenalin. These requirements would be satisfied by frogs' eggs and yeast cells as representatives of the animal and plant series respectively. Yeast cells are not particularly sensitive to acids, in fact, they form acids during fermentation. For the experiment 1-2 gm. of fresh pure yeast strains were suspended in acid and alkaline solutions, centrifuged, the supernatant liquid concentrated separately and glycogen estimated in each by Parnas's modification of Pflüger's method. Glycogen was always prepared as such and converted into sugar by hydrolysis, the former being estimated by Bertrand's method. The acid addition employed was hydrochloric acid and  $\text{NaH}_2\text{PO}_4$ , the alkaline addition  $\text{NaOH}$  and  $\text{Na}_2\text{HPO}_4$  in graded concentrations of  $\frac{1}{3}20$  to  $\frac{1}{6}$  normal. Each test was placed in the thermostat for two and a half hours at 37° C. The results were recorded in tables and curves. They showed that the glycogen content of yeast cells does not undergo regular alteration in acid mediums, as was to be foreseen in view of the known resistance to acid of these cells. Yeast cells enrich themselves in glycogen when suspended in alkaline solutions of low concentration. With higher concentrations still more glycogen is formed, the glycogen content in the yeast cells remaining constant or diminishing, while the glycogen values in the liquid rise very rapidly. Glycogen is, therefore, not retained by the cell, but is given off to the surrounding liquid. Consequently the increase of performed sugar into glycogen, because total carbohydrates appear to be increased in yeast after the action of alkali.

This increase of carbohydrate in yeast cells under the influence of alkali depends also, in part, on the transformation of albumin into carbohydrate, which seems to be confirmed by increase of rest nitrogen. But from the increase in carbohydrates and glycogen in the individual cell it may be concluded that the sugar-sparing action of the alkali on the liver cell is at least partly a direct cellular activity.

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**Some New Observations and Interpretations with Reference to Transportation, Retention, and Excretion of Carbohydrates.**

*Otto Folin and Hilding Berglund, J. Biol. Chem., 51:213, March, 1922.*

These experiments were begun for the purpose of determining the relationship between the elimination of sugar and the concentration of sugar in the blood. In order to throw additional light on the character of the carbohydrates in urine and blood the authors determined the sugar both before and after hydrolysis. In nearly all of the experiments the blood sugar was determined in plasma as well as in whole blood, both before and after hydrolysis. The volume percent of the corpuscles was determined by the hematocrit method. The (human) subjects of the experiments received one of the following substances: glucose, maltose, dextrin, starch, fructose, galactose and lactose. At various times after the administration, the urine and blood were carefully examined. The article also discusses the nature and origin of the sugar of normal urine; the nature of the glucose threshold; some observations on renal glycosuria; emotional hyperglycemia and glycosuria; subfasting blood sugar levels (hypoglycemia); and the distribution and character of the blood sugar. From this experimental work and tabulated data it is learned that in the absence of emotional complications or a subnormal threshold (renal glycosuria), the ingestion of pure glucose (up to 200 gm.), does not raise the level of the blood sugar above the threshold in normal persons, and no glycosuria is obtained. Fructose, galactose, or lactose, as well as dextrin or starch, were found to be much less effective than glucose in raising the level of the blood sugar. Absorption of sugars from the blood by the tissues, rather than glycogen formation, is believed to be the immediate reason why the sugar fails to accumulate in the blood. It is argued that a renal threshold analogous to that for glucose exists for fructose, but not for galactose or lactose. The retention and utilization of galactose depends on the amount of available glucose. Hypoglycemia (subfasting blood sugar level) is considered quite as normal a consequence of carbohydrate ingestion as hyperglycemia, but comes later. Hypoglycemia is probably a reflection or index of a decreased need for sugar transportation from one set of tissues to another. This condition is obtained when there is an abundance of carbohydrate material in all the tissues. A general abundance of other suitable food than glucose, notably fat (olive oil) may, therefore, also produce hypoglycemia. Hypoglycemia (in venous blood) can occur even during a prolonged moderate sugar absorption from the intestine, because the absorbed sugar may get by the liver, but does not get into the venous blood. Definite "glycuresis" (Benedict) is obtained after every ordinary carbohydrate meal, is independent of the level of the blood sugar and

is not normally obtained from the ingestion of pure glucose, maltose, dextrin or starch. It represents the absorption and excretion of (a) foreign unusable carbohydrate materials present in grains, vegetables, and fruits, and (b) decomposition products due to cooking, canning, and baking of such food. The sugar of normal urine consists, therefore, of a motley variety of carbohydrate products and carbohydrate derivatives including disaccharids and polysaccharids. The blood sugar is distributed in somewhat varying proportions between plasma and corpuscles. In fasting the distribution is nearly equal between the two. The plasma sugar is usually diminished by hydrolysis, while the sugar of the corpuscles is usually increased. The corpuscles probably contain polysaccharids, possibly polysaccharids other than glycogen.

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**Observations of Glyconeogenesis. I. Experiments in a Particular Case of Disturbed Carbohydrate Metabolism.**

*J. K. Parnas and Richard Wagner, Biochem. Ztschr., 127:55, Berlin, Feb. 28, 1922.*

Knowledge regarding neoformation of sugar from substances other than carbohydrates is based on experiments on surviving organs, particularly the blood-steeped liver, and on metabolism experiments with the pancreas in diabetic individuals or those poisoned by phloridzin. In the former case the increased sugar content of the glycogen deficient liver indicates glyconeogenesis. In the latter case the increased sugar excretion in a glycogen deficient individual after the administration of definite substances points to glyconeogenesis from the substance administered. Experiments have shown that among the amino-acids, glycocoll, alanin, glutaminic acid, leucin, cystin and asparagin are to be regarded as sugar forming substances, as also those fatty acids which do not form acetone, namely, lactic acid, glycerin, propionic acid, isobutyric acid, isocaproic acid and heptylic acid. Leo Pollack observed hyperglycemia in rabbits following administration of substances that had hitherto been viewed as mother substances of glyconeogenetic agents, though no similar hyperglycemia would be produced by sugar itself or by lactic acid. From this it was concluded that the action of these substances on the blood sugar value resembles that of adrenalin and this was supposed to find support from the fact that ergotamin abolishes the action of these substances.

It was attempted to study these questions on a girl, aged 9, who had a liver tumor and whose urine, in a fasting condition, was free from sugar and acetone. After ingestion of carbohydrate food, the blood sugar curve rose from 0.4%. After 5 A.M. glycosuria ceased, while during subsequent hours acetone was excreted copiously. This case was interpreted to show that the capacity for converting the albumin of the food into carbohydrate was preserved, while on the other hand the breaking down of tissue-albumin for purposes of carbohydrate formation, which takes place in severe diabetes, was absent. The process was therefore considered one of azo-amyl. Blood sugar values were determined while fasting, after carbohydrate feeding, and after adrenalin administration, and also the influence exerted on blood sugar values by albumin, nonnitrogenous substances and amino-acids. Adrenalin, the most powerful of the sugar-mobilizing stimuli, proved inactive.

Administration of exogenous albumin raised blood sugar to its normal value. Lactic acid acted as a strong sugar forming agent. The amino-acids and amino-acid mixtures were shown to represent the mother substances of the sugar forming agents. As regards glycogenesis from far it was possible to show that sugar could not be increased by administration of fat emulsions.

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**The Kidney Factor in Phlorhizin Diabetes.**

*Thomas P. Nash, Jr., J. Biol. Chem., 51:171, March, 1922.*

In order to dispose conclusively of the possibility that the phlorhizinated kidney produces, at least in part, the sugar which it excretes, it is essential to demonstrate not only a loss of blood sugar in passing the kidney, but a loss of such an order of magnitude as to account substantially for the excreted sugar. The author believed the question of sufficient importance to justify its reinvestigation. The experimental subjects were female dogs to which were given daily subcutaneous injections of 1 gm. phlorhizin in sterile olive oil. The experimental period in 6 of the 8 cases was extended over several days, in order to demonstrate the degree of glycuresis and to observe the development of the attendant hypoglycemia. The later animals of the series were fed meat in order to increase the total sugar output and thus, presumably, the difference, if any, between the sugar content of arterial and renal venous blood. Small (never more than 5 c.c.) blood samples were taken, following two hours of anesthesia, as nearly simultaneously as possible from the renal vein and the femoral or carotid artery. During this two hour period of anesthesia (ether) the urine was collected, its volume noted, and its sugar content determined. Blood sugar was measured by the modified method of Lewis and Benedict: urinary sugar by the Allihn method, weighing the copper as cupric oxid; total nitrogen by the macro Kjeldahl technic. Merck's phlorhizin was used. The author's tabulated results show that in phlorhizinated dogs the renal venous blood contains a lower concentration of sugar than the general arterial blood, provided the kidney function has not been abolished or seriously impaired. The kidneys, under the influence of phlorhizin, do not acquire a specific sugar-producing function. The author's results confirm an increased permeability of the renal epithelium.

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**The Localization of the Decomposition of Fatty Acids in the Organism.**

*Julius Baer, Biochem. Ztschr., 127:275, Berlin, Feb. 28, 1922.*

In order to recognize the conversion of chemical substances in an organ, that organ must be excluded from the otherwise intact organism, or the influence of isolated blood-steeped organs must be examined. The question was investigated whether decomposition of fatty acids takes place after decomposition in the liver. The experiments were carried out on the frog, in which extirpation of the liver is easily performed. Butyric acid was selected for the researches as it permits decomposition or oxidation in the beta position. In the frog aceto-acetic acid, i. e., acetone, could not be detected as a normal secretory product. But neutralized butyric acid injected into the animal was

oxidized to oxybutyric acid and aceto-acetic acid in the manner common to mammals. Aceto-acetic acid was detected, though only in small amounts, from which it was concluded that aceto-acetic acid is very easily decomposed. It was also shown that aceto-acetic acid is destroyed in large amounts by normal living frogs. Beta-oxybutyric acid is to be regarded as the intermediate product in the oxidation of butyric acid to aceto-acetic acid in mammals. The injection of beta-oxybutyric acid showed that the hepatectomized frog is able to oxidize beta-oxybutyric acid to aceto-acetic acid the same as the normal frog. Both the normal and the living frog destroyed or converted butyric acid in considerable amounts. Destruction or resorption of aceto-acetic acid, or oxidation of oxybutyric acid to aceto-acetic acid, is not determinable in the frog's skin, but resorption of butyric acid into the skin seems to take place though it is disturbed in the hepatectomized frog. The results of the researches are, for the present, valid only for the frog.

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**Calcium in Egg-Shell Formation.**

*G. D. Buckner, J. H. Martin, W. C. Pierce and A. M. Peter, J. Biol. Chem., 51:51, March, 1922.*

In connection with an experiment dealing with the Ca, Mg, and P metabolism in the laying hen, 6 lots, each containing ten 7 months old white leghorn pullets which came from the same parent stock, hatched the same day, and existing under identical conditions, were fed the following feeds: Lot 1, grains and tankage with no mineral material. Lot 2, grains, tankage and granite grit, ad libitum. Lot 3, grains, tankage, granite grit and oyster shell ad libitum. Lot 4, grains, tankage, granite grit and limestone ad libitum. Lot 5, grains, tankage and limestone ad libitum. Lot 6, grains, tankage and rock phosphate, ad libitum.

Tankage containing 6.4%  $P_2O_5$  was fed in the dry mash. The grit contained 2.4% CaO soluble in strong HCl. The experiment was started Dec. 1, 1920, and ended Aug. 1, 1921. During this period the pullets were confined in houses and at no time allowed access to the ground, thereby excluding any chance of their obtaining calcium-containing materials from undesired sources. No milk or green foods were fed. At the beginning of the experiment 2 representative birds were killed and after their femurs and tibias were dissected out and separately weighed, the  $CO_2$  free ash and CaO contained therein were determined. A hen of the same age, having received the same treatment as all other birds in this experiment up to Dec. 1, 1920, but which had from that time until Aug. 1, 1921, been allowed the normal freedom of a meadow and been fed the same as Lot 3, was killed and similarly dissected as were the early controls just mentioned. All the birds remaining in the 6 lots on that date were killed and treated in the same way. A trapnest record was kept of each bird confined. Among other things the carbon-dioxid-free ash and the percentage of CaO in this ash were obtained in a composite sample of the shells of the first three eggs laid each month by each hen. The tabulated results, which represent averages, show that the total weights of the 4 large leg bones of the hens in Lots 1, 2, 3, 4, 5, and 6 were approximately the same while that of the first control was lighter, being eight months younger and that of the second control was heavier, resulting from the different physical condi-

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tions governing the eight months over which this experiment extended. The actual weight of the carbon-dioxid-free ash of the leg bones from Lots 1 and 2 was lighter than that from Lots 3, 4, 5, and 6 which received the concentrated calcium materials, and the ash from Lot 6 which received rock phosphate was heavier than that from any of the other lots. The table also shows that Lot 1, which received no mineral matter in addition to the grains and tankage fed, laid 19.9 eggs per hen in eight months which is slightly in excess of the number laid by Lot 6 which received the rock phosphate ad libitum. This might indicate, when considered with the previous statement, that the rock phosphate can be utilized by the hen in bone formation but not in the production of eggs, calcium being the limiting factor in the case under consideration. This is shown by the fact that the average weights of the carbon-dioxid-free ash and the CaO in the egg-shells of Lots 1, 2 and 6 are practically the same while those in Lots 3, 4, and 5 are larger. It was observed that the percentages of CaO in the carbon-dioxid-free ash of the egg-shells was practically constant in all lots.

From the results obtained in these experiments it appears that the hen can utilize the calcium in calcium carbonate for the production of both egg-shell and bones but that the calcium in tricalcium phosphate can be utilized only for the growth of bone and not for egg-shell production. Finally, calcium starvation is not the determining factor in the production of shell-less eggs.

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#### The Behavior of Blood Sugar at Different Ages after Administration of Glucose by Mouth.

*Wilhelm Loeffler, Biochem. Ztschr., 127:316, Berlin, Feb. 28, 1922.*

The direct fate of ingested carbohydrates is exactly measurable by blood sugar and respiratory metabolism. A constant quantitative relationship between alimentary glycosuria and blood sugar level has not been established as yet because there are no methods sufficiently delicate to determine physiologic, and frequently also alimentary, sugar elimination in urine, and because no typical behavior of blood sugar during normal processes of digestion can be observed.

The behavior of blood sugar was investigated in various old persons immediately after glucose ingestion. Following administration of glucose to healthy adults a regular and considerable increase in blood sugar occurred. The results of a large number of experiments showed, on an average, a fasting blood sugar value of 0.096%; 20 gm. glucose caused an average increase of 0.137%, and a maximum increase up to 49%. The rise in blood sugar was noticeable ten minutes after ingestion, reaching its highest point in about half an hour and subsiding in one or two hours. In old persons fasting blood sugar was increased 20%—30% above that in juveniles. From age 58 to 70, fasting blood sugar amounted to 0.106%, the maximum rising to 0.152%, this maximum being about 43% higher than the initial value. In individuals over 70 the fasting blood sugar lay at about 0.111%, the maximum at 0.165%, which represented an increase on the fasting value of 48%.

While in juveniles the fasting value is again attained in seventeen minutes, nearly twice this time is required in old people: In  
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diabetic patients hyperglycemia persists a remarkably long time and the decline to the fasting value in these patients is very slow. The importance of glycemia to the organism is therefore determined by a combination of both factors namely, height and duration of the increased blood sugar value. Height and duration are also influenced by the amount of ingested glucose. In pregnancy a remarkably low blood sugar value is found; this is due to the increased permeability of the kidneys for sugar in these patients. Alimentary renal glycosuria therefore serves diagnostically as one of the earliest signs of pregnancy.

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**The Influence of Carbonic Acid on Blood Sugar in the Organism.**

*Friedrich Binswanger, Pflüger's Arch. f. d. ges. Physiol., 193:296, Berlin, Feb. 9, 1922.*

The hyperglycemia observed by Claude Bernard following stimulation of the central stump of the pulmonary vagus branches could be referred to the mechanism: stimulation of the pulmonary branches of the vagus nerve by the carbonic acid, of the glycogenic center, then of the splanchnic nerves, of the glycogen depot of liver cells, leading to sugar discharge. This assumption cannot be explained experimentally.

On the other hand interesting points presented themselves regarding the question whether the action of carbonic acid leads to hyperglycemia, whether the appearance of the latter is related to any regulatory processes and, regarding the mechanism of such hyperglycemia. In the experiments the corresponding oxygen content of the carbonic acid mixture was taken into consideration. The experiments on rabbits, cats and dogs showed that the addition of carbonic acid to the inspired air in a certain concentration leads initially to hyperglycemia. This carbonic acid hyperglycemia is, therefore, a fixed and demonstrable fact. A relationship to a governing mechanism in carbohydrate metabolism could probably be established if fluctuations in the production of carbonic acid, for instance under intense muscular work, manifested themselves also by fluctuating concentration in the lung. As a matter of fact, muscular work produces fluctuations of carbonic acid concentration in the alveoli which depend not only on the production of carbonic acid but also on the degree of acidity of the organism. But the reduction of carbonic acid tension in the blood does not affect the blood sugar content. The phenomena of the central nervous and sympathetic systems that occur almost simultaneously with increase of blood sugar (salivation, dilated pupil, rise in blood pressure) point to material participation of the glycogenic center. As carbonic acid hyperglycemia ensues even after bilateral division of the splanchnic nerves the stimulus probably acts peripherally from the glycogenic center. Carbonic acid hyperglycemia was produced even when the spinal cord was divided at the level of the second or third dorsal segment in the cat, or the second segment in the rabbit, and likewise after bilateral exclusion of the vago-sympathetic trunk. Removal of the pancreas or of the suparenal glands did not influence the phenomenon. Consequently the only possible remaining attacking points for carbonic acid are the celiac ganglion with its peripheral extensions and the liver cells. It is improbable that acidity plays any rôle in this process inasmuch as no increase in ammonia elimination is detectable

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even in prolonged experiments. An explanation may perhaps be afforded by the fall of 2° to 3° in body temperature during the experiments, if the same be interpreted as an expression of diminished oxidation and hence of reduced sugar consumption.

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**The Influence of Amino-Acids and Fatty Acids on Blood Sugar Regulation.**

*Leo Pollak, Biochem. Ztschr. 127:120, Berlin, Feb. 28, 1922.*

These experiments to determine which products of albumin and fat metabolism are converted into glucose or glycogen in the organism were carried out on animals suffering from so-called total phloridzin diabetes, or on pancreatectomized dogs. Such animals received amino-acids or fatty acids whose conversion into glucose was deduced from the surplus sugar calculated from the quotient of D: N. The experiments show that certain amino-acids, such as glycocoll, alanin and asparaginic acid, produce distinct hyperglycemia in normal rabbits when injected subcutaneously in amounts of 1 gm. Leucin is inactive while a 5% solution of Witte's peptone has the same positive effect. Saturated fatty acids having an odd number of carbon atoms also increase blood sugar, whereas fatty acids with an even number of carbon atoms are inactive in this respect (acetic acid, normal butyric acid, isovalerianic acid, normal caproic acid). The behavior of fatty acids is therefore directly contrary to that in the formation of acetone bodies in the surviving liver. The intensity of the glycemia induced by the foregoing substances depends on the animals' glycogenic condition and may be obviated entirely by previous simultaneous injection of an ergotoxin preparation. This proves the existance of a stimulating action on glycogen decomposition in the liver by decomposition products of albumin and fatty acids. It is probable that amino-acids and fatty acids do not, as such, exercise the stimulating effect which is due rather to conversion products of the same, possibly ketone acids. In this process definite amino-acid derivatives may produce stimulation, others conversion into sugar. In the case of alanin, transition into pyroracemic acid and into lactic acid in the animal body has been demonstrated. But pyroracemic acid causes hyperglycemia by stimulation, while the conversion of lactic acid into sugar has been repeatedly established.

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**Further Study of the Permeability of the Glomerulus Membrane to Stereo-Isomeric Sugars, Especially Galactose.**

*H. J. Hamburger, Klin. Wchnschr., 1:418, Berlin, Feb. 25, 1922.*

Perfusion experiments have demonstrated that the glomerulus membrane of the frog's kidney may hold back glucose in the amount physiologically present in the blood, while other crystalloids and substances, with two and three times the molecular weight pass through. Isomeric fructose and mannose are not held back and other stereo-isomeric hexoses only partially, including d-galactose (50%) and xylose (25%). In aqueous solutions, d-galactose occurs in 2 forms, one of which is held back and the other not. The glomerulus membrane can separate two kinds of sugars quantitatively, for instance a mixture of

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glucose with levulose or lactose. The author thinks these observations give an excellent physiologic picture of the hypothesis of stereo-isomerism, and indicate that multirotatory sugars should be considered biologically as monomorphic substances

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**The Effect of Flood Diuresis on Hemoglobinuria.**

*Herbert Haessler, J. Exper. Med., 35:515, April 1, 1922.*

The fact is well recognized that a considerable quantity of hemoglobin must be free in the plasma if any is to pass the renal barrier and appear in the urine. The pigment is, like dextrose, a threshold substance. It readily penetrates into the renal tubules but is absorbed again more or less completely during its course through them. This being true, diuresis should diminish the chances of absorption by hastening the flow of fluid, and tend to lead to the appearance of the pigment in the urine. Hemoglobinuria, like glycosuria, is much favored by flood diuresis. The tubules of the rabbit kidney are much less active in resorption than those of human beings; yet when very large quantities of water are administered to this animal even its feeble power of absorption is sufficient to save the optimal fluid. The present findings have no bearing on the occurrence of clinical hemoglobinuria. They are not without significance, however, for a proper understanding of the renal siderosis that occurs in diseases which involve the repeated liberation of small quantities of blood pigment into the circulation. The writer concludes that flood diuresis so far lowers the renal threshold for hemoglobin that the pigment appears in quantity in the urine as result of a hemoglobinemia insufficient under ordinary circumstances to lead to the elimination of even a trace of it. In pathologic conditions that involve blood destruction, hemoglobin probably passes into the tubules much more often than it reaches the urine, being prevented therefrom by the resorptive activity of the tubular epithelium.

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**The Renal Elimination of Bilirubin.**

*Herbert Haessler, Peyton Rous and G. O. Broun, J. Exper. Med. 35:533, April 1, 1922.*

The mode of escape through the kidneys of circulating blood and bile pigment has received only scant attention in the past as compared with that of foreign dyestuffs. The urinary sediment of many icteric human beings and of dogs has been studied with jaundice produced in several ways. Two types of cell staining with bilirubin have been discriminated, one consequent on sojourn of the elements in the urine, the other a direct expression of the renal condition. The cells of manifest renal origin may be deeply stained. The specific pigmentation of the renal cells is most evident in specimens freshly voided; and some hours are required for the bilirubin to dissolve out of the more heavily impregnated cells. After long continued jaundice in man, the urinary sediment yields striking indications of the serious condition of the kidneys. It was found that the elimination of bile pigment during jaundice is, for practical purposes, not increased by diuresis from water by mouth. Possibly the flushing of the kidneys tends to lessen pigment accumulation within these organs and thus to diminish a serious potential source of

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trouble in long continued jaundice. Flood diuresis from intravenous injections of salt solution brings out a relatively considerable quantity of bile pigment. It is important to know the effect of variations in the urinary output on the elimination of bile salts, but methods for the purpose are not available at present. The passage of bile pigment into the kidney cells during jaundice is attested by the presence in the freshly voided urine of desquamated renal elements specifically stained, stippled, or granulated with bilirubin. Pigmentation of this sort is readily to be distinguished from the indiscriminate staining of cellular débris that occurs in icteric urines on standing. It has clinical significance, furnishing direct evidence on the degree of renal change.

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**Decomposition of Bile-Pigments by Anaërobic, Septic Intestinal Bacteria.**

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*Fritz Passini, Wien. klin. Wehnschr., 35:217, March 9, 1922.*

Chemical reducing substances transform bilirubin into a colorless substance, hemibilirubin which is identical with the urobilinogen, found in urine. The pigments produced in the liver, bilirubin and biliverdin, are reduced in the intestinal tract to a leuko-pigment, a definite chemical substance, from which by oxidation urobilin is produced, and a mixture of condensation products appears. In hemorrhages and hemolytic processes larger amounts of these substances can be detected in the urine. The liver decomposes the blood-pigment into hemin and albumin, and oxidizes hemin to bilirubin, which when secreted into the intestinal tract undergoes the same reactions of reduction. It is quite probable that the liver takes a part in the transformation of bile-pigments into urobilin; it also takes part in the production of urobilinuria in so far as in a diseased condition it is unable to keep the decomposition products of bile-pigments, which it receives from the intestine, out of the blood circulatory system, and is still less capable of transforming them.

But even the normally functioning liver does not seem to be in a condition either to decompose further the reduction products which it received from the intestine, or to transform them back into the pigment; this assumption is corroborated by the constant discovery of urobilin and urobilinogen in the gall-bladders of persons who for some outside cause had died when perfectly healthy. Only the bile of new-born infants is free from biliary decomposition products; apparently it does not give the urobilin and urobilinogen reactions because in the bacteria-free intestinal tract no transformation of the bile-pigment takes place, and, therefore, no decomposition products reach the liver. The bacterial transformation of bilirubin into hemibilirubin (urobilinogen) probably proceeds in that the organisms in the oxygen-free intestine need for their growth oxygen and withdraw the required quantity from the existing nutrient matter. There is also the possibility that the nascent hydrogen produced by the anaërobies causes the reduction of bilirubin, or that the bacteria produce fermentations which have the power of transforming the bile-pigments. As no experiments had been made to study the effects of pure cultures of anaërobically growing, putrefactive bacteria upon the pigments contained in liver secretions, Passini undertook such experiments with *Bacillus putrificus Bienenstock*, a typical bacterium which causes the putrefaction of albuminous bodies, using the bile of persons

who either had died suddenly or had been killed in an accident, and whose autopsy was undertaken immediately after their death. The experiments yielded the following conclusions: (1) The putrefactive, anaerobic bacteria decompose biliverdin and bilirubin in a very short time. But it could not be proved that they are transformed into either urobilinogen or urobilin. (2) The pigments may be changed, partly at least, by the fermentations which these anaerobes produce. (3) The presence of sugar in the cultures of typical putrefactive bacteria does not prevent the disappearance of the bile-pigments, while the species of anaerobes which cause fermentation of substrata containing sugar have not the slightest influence upon bile-pigments during the period of their growth. So far as the occurrences in the intestinal tract are concerned, it may, therefore, be safely assumed that in those parts of the intestine where, on account of the presence of fermentative materials, the ferment producing anaerobes exhibit their chief activity, the bile-pigments are not changed at all; but that in the deeper regions, where putrefaction predominates, biliverdin and bilirubin disappear, or are transformed into a still unknown product. The transformation of these pigments into urobilinogen and urobilin is probably caused by factors in the intestinal canal other than the putrefaction produced by anaerobes, since this seems to cause only their disappearance.

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**The Significance of Phosphoric Acid in Muscle Physiology.**

*E. S. Schmitz, Klin. Wchnschr., 1:432, Berlin, Feb. 25, 1922.*

The significance of phosphoric acid in muscle activity was first explained by studies on isolated muscle substance. Embden and Grawe then showed on human subjects that active muscle work always leads to increased excretion of phosphoric acid in the urine. Later Siegfried showed that on the breaking down of phosphocarnic acid both phosphoric acid and lactic acid were produced. The mother substance of lactic acid found in muscle and named by Embden, lactacidogen, was found to be a close combination of phosphoric and lactic acids, the essential constituent of which was a hexose phosphoric acid. While the formation of lactic acid and phosphoric acid in skeletal muscle is very considerable, it is less in heart muscle and there is only a trace of it in smooth muscle. These facts raised the question of the physiologic significance of lactacidogen. It seems that an abundance of lactacidogen indicates a condition of increased functional capacity, that it is the driving substance of muscle. Hexose phosphoric acid is an intermediate product in the catabolism of carbohydrate in muscle. According to this theory an increase in phosphoric acid would increase the functional capacity of the muscle. Experiments with troops, in factories and in mines, showed that a considerable increase of physical strength and psychic vigor was brought about by the administration of phosphates. Animal breeders found, too, that when the strength of their horses had been reduced by the use of grain substitutes as food, they had good results from the administration of sodium biphosphate. A good form of sodium biphosphate is "recresal," which has been reported upon favorably by Adam, von Noorden and others.

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The Total Energy Curve of the Tetanized Frog Gastrocnemius and the Portion Physiologically Utilized.

Otto Beck, *Pflüger's Arch. f. d. ges. Physiol.* 193:495, Berlin, Feb. 22, 1922.

Thus far, no systematic investigations have been carried out on the relations between the initial tension of a muscle and the increase of tension in tetanus. It is necessary in this connection to determine what part of the total tension curve is utilized by the animal organism when the initial muscle lengths vary. To judge these conditions, the term "natural length" of the muscle must be accurately defined. It can refer only to the condition of the muscle when free from any deformity. In order to exclude any influences favoring deformity, in this experiment, the nerves and tendons of all antagonistic muscles were cut. The tests were carried out with the gastrocnemius muscles of well-developed frogs, the isometric tension during tetanus being registered by means of one lever, and the change in length by a second lever. The experiments were performed in part with excised muscles, in part with attached muscles having good circulation; after section of the ischiatic nerve. The highest total tension and the greatest increase in tension within the limits of physiologic movement of the joint is produced by indirect tetanic stimulation of the muscle, when the preparation is in a state of full physiologic stretching, i.e., when the foot is dorsoflexed and the knee is nearly extended. After section of the tendon, a relative maximum of total tension and the absolute minimum of increase of tension result if the original tension is still higher. When stretching is carried further, the total tension curve shows a minimum, followed by sudden rise. The curve of tension increase, however, falls steadily to 0 (with fullest possible extension) when the maximum has been passed, which coincides approximately with that of the total tension.

The second rise of the total tension curve is produced by the markedly increasing initial tension. Allowing for certain corrections, chief among them the after-tension of the muscle subsequent to isometric tetanus, it will be found that the highest obtainable physiologic increase of tension coincides with the absolute maximum, or at least closely approaches it. The law which A. Fick has discovered, and which shows that with increasing length over the "natural length" a relatively high tension maximum is obtained in a limited area, during isometric spasm, has been verified for isometric tetanus. Within the limits of physiologic joint action it is true that with increasing length beyond "natural length" (which for the frog is about the position of equinus) total tension and increase of tension will rise. According to Franke, human muscles act otherwise; in them the maximum of power is exceeded before the physiologic length is reached. Tension and length are not exactly proportional; total tension and tension increase are functions of muscle length, but do not run parallel with it. Within certain limits, however, the total energy (heat production and mechanical work) and initial length are proportional. The possible energy of the muscle is utilized in the animal organism for short distances only; the muscle can produce considerable work with a smaller mass than the smallest amount which exists in the body and with a degree of stretching exceeding the physiologic. Thus the frog gastrocnemius utilizes only  $\frac{1}{4}-\frac{1}{5}$  of the total possible path of shortening, and only  $\frac{1}{3}$  of the path of

shortening lying between the length of the greatest tension increase and the shortest length. The absolute energy is the state of maximum tension, in relation to the unit of cross section of the muscle, which was obtained with maximal stimulation and most favorable initial length. This represented a maximum energy of 1.83 kg. per square centimeter; with natural length 1.1 kg. per square centimeter were obtained.

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**The Formation of Inorganic Phosphoric Acid in the Contraction of Frogs' Muscle.**

*Gustav Emden and Heinz Lawaczeck, Biochem. Ztschr., 127:181, Berlin, Feb. 28, 1922.*

In accordance with the occurrence of equimolecular amounts of phosphoric and lactic acids on warming, for a short time, fresh expressed juice from dog's skeletal muscles, a substance resembling hexose, phosphoric acid was obtained. For the decomposition of carbohydrates in the muscles, as for alcoholic yeast fermentation, their previous linking to phosphoric acid must manifestly be presupposed. It is obvious that phosphoric acid is liberated from the lactacidogen molecule, besides lactic acid, during muscular activity at the moment of contraction. But, as the amount of phosphoric acid is not increased even with prolonged stimulation, the free phosphoric acid is regenerated to lactacidogen by synthesis with carbohydrate, while lactic acid accumulates, as it cannot be removed with sufficient rapidity in the isolated muscle. The fatigue of the frog's leg, therefore, can not arise from the simple consumption of the activating substance (assumed to be lactacidogen), but must be due to other circumstances.

Researches were carried out on gastrocnemius muscles which were fastened between copper electrodes and immediately stimulated faradically. One of the muscles was contracted maximally and dipped in liquid air in which it congealed quickly. The other muscle was stimulated further and then frozen in the same way after corresponding fatigue. The further preparation of both muscles and estimation of inorganic phosphoric acid followed. Phosphoric acid was estimated as strychnin phosphomolybdate and corresponded to 39 times the weight of phosphoric anhydrid or 28 times the weight of phosphoric acid present. The researches were recorded in tables and showed conclusively that muscular activity is attended, not merely by splitting off of lactic acid, but also by splitting off of inorganic phosphoric acid. Both acids are derived from lactacidogen. The phosphoric acid formed during muscular contraction is rapidly reconverted into the organic form. Numerous facts support the view that, in addition to exothermic chemical reaction of lactacidogen decomposition, an exothermic physiochemic process takes place at the moment of contraction. This physiochemic exothermic reaction manifests itself by intumescent processes under the influence of suddenly increased hydrogen-ion concentration. Greater importance may be ascribed to the more strongly dissociating phosphoric acid in the process of muscular contraction than to the less strongly dissociating lactic acid. While lactic acid accumulates up to a certain maximum in every prolonged stimulation of isolated frog muscle, the inorganic phosphoric acid is not increased perceptibly after contraction. Phosphoric acid is therefore confined to contraction, as to time, much more so than lactic acid. At any rate the experiments seem to prove that

the contraction of isolated frog muscle not only causes formation of lactic acid, as is well known, but that inorganic phosphoric acid is liberated from lactacidogen, the phosphoric acid so liberated being reconverted into lactacidogen very quickly after contraction, or probably even during the continuance of the state of contraction.

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**Alteration of the Cholin Content of Frog's Musculature by Electric Stimulation.**

*E. Geiger and O. Leewi, Biochem. Ztschr., 127:174, Berlin, Feb. 28, 1922.*

In frogs whose suprarenal glands had been removed the cardiac poisoning symptoms could be accelerated by means of intense electric stimulation of the whole animal. This might be due to an accumulation of cholin in the blood. Experiments were therefore undertaken to determine whether intensive muscular stimulation leads to increase of cholin in normal frogs' muscles. For the preparation of cholin, Reid Hunt's method was employed, absolute alcohol replacing acetone for extraction. The collected alcoholic extracts were evaporated to dryness, acetyl chlorid added and acetyl ester prepared in this way. The experiments were commenced with barely active concentrations and carried through on the hearts of *Rana esculenta*. It was possible to show that stimulation of the gastrocnemius muscles produces an increase in their cholin content.

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**Intracellular Oxidation and "Nadi" Reaction.**

*Siegfried Graeff, Beitr. z. path. Anat., 70:1, Jena, Feb. 14, 1922.*

When a colorless mixture of naphthol and dimethyl-p-phenylendiamin is brought in contact with an excised striated muscle, a blue coloration of the muscle begins to appear within a few minutes. This starts from the edge and progresses so rapidly that within ten or fifteen minutes a piece about the size of a pea shows distinct bluing. With powerful magnification it can be seen under the microscope that this macroscopic color change depends upon the formation of very fine dark blue granules which are regularly distributed throughout the cell protoplasm, the arrangement depending upon the tissue in question; the nuclei are always free from these granules. Other tissue cells, such as liver, kidney, ganglion cells, leukocytes and spermatozoa give a reaction like muscle cells, while connective tissue cells, glia cells and other supporting tissue cells react very feebly. Embryonic tissue reacts in direct ratio to its age. It is a striking observation that the musculature of the pregnant uterus shows a more intense reaction than that of the resting organ. In tests carried out with the pale and the dark-colored muscle of rabbits, the dark muscles always showed a more rapid and more intense reaction. Some vegetable cells, bacteria and amebas react in the same manner. Since this reaction is independent of the morphologic structure of the cell, Graeff considered the possibility of its being connected with cell function. He studied the end of this oxidation reaction using striated muscle from man and animals. His reagents were a 10% alcoholic solution of naphthol diluted 100 times with distilled water, and a 0.5% aqueous solution of dimethyl-p-phenylendiaminchlorid. The mixture of the two solutions is designated as nadi mixture, and the reaction a nadi reaction.

An accurate analysis of the course of reaction under different conditions shows that alterations depend upon an oxidase, which must be considered as the agent producing synthesis. This oxidase the author terms phenolase, or polyphenoloxidase. This reagent stimulating the synthesis of indophenol blue shows remarkable analogies to the ferments. It appears from certain facts in morphology, physical chemistry, toxicology and physiological chemistry, of healthy and diseased cells of animal and vegetable organisms that the final outcome of the nadi reaction depends upon functional differences of the surviving cells, and that the reaction furnishes a reliable index of the oxidative efficiency of the living cells; it must, therefore, be regarded as a valuable biologic reaction. The agent stimulating oxidation shows toward poisons the same behavior as the substance which Warburg has recognized as the catalyzing factor of respiration—iron.

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**The Influence of the Nerve Supply on the Capacity of Muscles for Intravital Staining.**

*E. Magnus-Alsleben and P. Hoffmann, Biochem. Ztschr., 127:103, Berlin, Feb. 28, 1922.*

Intravital staining has been employed frequently from various points of view. By means of it Ehrlich studied the oxygen requirement of the body. Thunberg utilized the action of the tissues in decolorizing methylene-blue for examining intermediate metabolic products and the enzymes formed during this process. In the course of an investigation of the influence of the nervous system on inflammatory processes it was found that when methylene-blue is injected into frogs whose peripheral nerves had been divided, the paralyzed musculature is stained blue, while the whole of the other muscles remain colorless. This is shown best if injection is performed after division of the nerves and the animal is killed one or two days later. Injection of carmin, trypan-blue and iso-min-blue did not act similarly.

The question arises whether the musculature of the paralyzed limb is, in reality, the only one that retains the dye, or whether the other muscles also contain it, but in a reduced and therefore colorless state. Further, is muscular rest the sole cause of the different behavior, or must other factors be assumed to result from nerve division? The customary method, viz., the conversion of the leuko base of methylene-blue into the dye by simple suspension in air, or by the action of hydrogen peroxid, gives a negative result. Under these conditions normal musculature is colorless. Normal colorless muculature dipped for a brief period in dilute acids ( $3\text{--}4\%$  HCl or  $\text{H}_2\text{SO}_4$ ) gradually assumed an intense blue color. From this it seems certain that methylene-blue is stored in all muscles, in paralyzed muscle as ordinary methylene-blue, and in normal muscle in its reduced state. The leuko base exists in the form of a combination which is split easily by dilute acids. In the researches hitherto carried out the basic methylene-blue dyes showed no difference between active and resting muscles. In both cases the dyes were reduced. When the paralyzed muscle was activated faradically the musculature remained blue and no reduction followed forced muscular activity. Therefore it is possible to determine by means of intravital staining with methylene-blue whether the muscles of a cold-blooded

animal are connected with the central nervous system and this at a time at which no trace of muscular degeneration can be observed electrically. Hence, artificial stimulation is incapable of replacing the normal influence of the nerves on the chemical processes in the muscles.

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**The Ionic Theory of Stimulation and Pflüger's Laws.**

*P. Lasareff, Pflüger's Arch. f. d. ges. Physiol., 193: 231, Berlin, Feb. 9, 1922.*

For minimal stimuli, the formula  $C_1 \div C_2 = K^1$  has been devised in which  $K^1$  is constant and  $C_1$  and  $C_2$  represent the concentration of stimulating and stimulation arresting ions. This law was valid for threshold stimuli. It was found empirically by J. Loeb for the influence of solutions of salts on nerves and muscle and deduced by the author for general use. It is the fundamental law of stimulations in living tissue. If in a normal unstimulated condition the equation is  $C_1 \div C_2 = K_0$ , and in order to produce a stimulus  $K^1 > K_0$  then with the increase of  $C_1 \div C_2$  irritability will also be increased, whereas with a decrease in value, irritability will diminish. In the passage of a constant current through a tissue ions with greater motility overtake the less motile ones and the ionic proportion is subjected to displacement. According to Loeb's researches the more motile potassium ions stimulate the tissues while the motility arresting Ca and Mg ions lag behind. Therefore the value  $C_1 \div C_2$  must increase at the cathode toward which these ions travel, whereas contrary conditions are produced at the anode, owing to the relative lagging of Ca and Mg ions. In accordance with this, irritability must increase at the cathode and decrease at the anode. It is easily seen that when the circuit is closed the stimulus must first become active at the cathode while interruption causes activity at the anode. It is possible to show that on these assumptions all facts of Pflüger's laws may be deduced mathematically. The indifferent point, at which irritability corresponds to the normal condition, is found to coincide with the half-way point of the interpolar space, while it is actually displaced toward the cathode with increase of current strength. This is explained on the one hand by the varying dependence of ionic diffusion and on the other by alterations in the number of ions brought about by stronger currents.

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**The Relations of the Current of Rest to Irritability. II. Experiments on the Frog's Spinal Cord.**

*Hermann Voelkel, Pflüger's Arch. f. d. ges. Physiol., 193:313, Berlin, Feb. 9, 1922.*

In these experiments the degree of irritability was measured by the reflex irritability of the preparation (isolated spinal chord with ischiatic nerve and leg belonging thereto) induced by pinching the toes. The cross section of the spinal cord is always electronegative toward the longitudinal section. The opposite behavior observed occasionally (Beck) is due to contact of the electrode of the longitudinal section with the cross sections of the divided lumbar plexus. Narcosis, the same as in nerve and muscle, acts in the sense of a negation of the point of attack. Dabbing the spinal cord with 0.1% strychnin solution increases

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es the current of rest and irritability. A 1% cocaine solution increases the current and diminishes irritability while a 0.2% solution increases both phenomena. In any case the current of rest and irritability are found to be independent of each other inasmuch as the former is always increased and the latter is increased or diminished according to the strength of the alkaloid. The conception of the increase of the current of rest as an expression of the electromotive force of ganglion cells (Baglioni) is therefore untenable.

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**Variations in the Stimulation of Nerves Due to Differences in the Distance between the Electrodes.**

*E. Lapicque and H. Laugier, J. de physiol. et de pathol. gén., 19: 528, no. 4, Paris, 1922.*

The variations in the stimulation-effect produced by varying the distances between the electrodes were originally explained by the theory of electrotonus. Nernst's theory of polarization, the accumulation of salts or ions about a semi-permeable membrane, appears to be less preferable than the older theory. The diminution of stimulation produced by lessening the distance between the electrodes is readily explicable by reciprocal neutralization of opposed polarizations, interpreted by the theory of electrotonus.

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**The Action of Potassium Salts on the Medulla as Shown by Perfusion of the Medulla of the Terrapin (*Pseudomys Troostii*) with Potassium Salts.**

*W. J. R. Heinekamp, J. Pharmacol. & Exper. Ther., 19:239, April, 1922.*

The ionic action of potassium is manifested most generally by depression of the central nervous system. Hooker and Mathison, however, have brought forward evidence that potassium stimulates the medullary and spinal centers. In a series of experiments which were done to determine the action of various substances on the cardio-inhibitory center of the terrapin, potassium bromide was found to exert a marked influence on this center, resulting in complete or partial inhibition to the heart. Subsequently a series of experiments was performed to determine whether the potassium or the bromide ion was the causative agent. Results obtained indicate that the potassium ion is the causative agent, since sodium salts and magnesium iodide were without effect, while the corresponding potassium salts produced inhibition. In practically all cases 1:1000 solutions were used. The medulla was thoroughly washed out with amphibian Ringer solution which contained 0.03% potassium chloride and which in no case influenced the medullary centers.

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**Cortical Motor Mechanism of the Sheep Brain.**

*Charles Bagley, Jr., Arch. Neurol. & Psychiat., 7:417, April, 1922.*

One of the first fissures to develop in the neopallium in the sheep embryo, is the coronal sulcus. Lamination of the cortex mesial and lateral to the coronal sulcus is well marked at a stage of development (Sec. 1—Page 859)

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when the coronal sulcus has all the characteristics of the sulcus of the adult sheep brain. At this stage the layer of the large pyramidal cells extends throughout the superior frontal convolution and through the mesial portion, but does not reach the crest of the middle frontal convolution. Bagley's histologic findings in the superior frontal convolution are identical with those described by King; and in addition the cortex of the middle frontal convolution and that surrounding the outer extremity of the cruciate sulcus also present somewhat the same appearance. Stimulation of the posterior portion of the superior frontal gyrus produces contractions of the limbs. The cortex of the gyrus immediately in front of this area when stimulated causes movements of the head and eyes to the contralateral side. Stimulation of the most anterior portion of the superior frontal gyrus gives no reaction. Stimulation of the small gyrus between the frontal end of the presylvian fissure and the outer anterior spur of the coronal sulcus causes contraction of the facial muscles of the opposite side, especially of the lower lip. Stimulation of the middle frontal gyrus over an area of about 1 cm. square, usually opposite the middle portion of the coronal sulcus, but sometimes slightly more anterior, causes contraction of the facial muscles of the same side. This center is easily excited, usually requiring less current than is necessary in the other areas. Stimulation of the gyrus surrounding the outer extremity of the cruciate sulcus produces no reaction, notwithstanding its motor pattern. There is no response to stimulation of areas posterior to the cruciate sulcus. After extirpation of the excitable areas of the cortex, there is no disturbance of locomotion. The course of the main mass of the pyramidal tract, its decussation in the hind-brain, and disappearance in the upper cervical segments of the spinal cord, is the same as that described by other workers. In addition to the main mass of pyramidal tract degeneration, there is, however, in the tegmentum, evidence of the degeneration of a bundle of fibers. This degeneration, ipsilateral in its entire course, is first noticed in frontal sections at the level of the red nucleus, where the degeneration is followed dorsalward from the pyramidal tract to the dorsolateral angle of the tegmentum, ending at the level of the facial nucleus, beyond which it could not be demonstrated. No decussation to the extra-lateral nucleus was noted.

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**A New Theory for the Material Basis of the Functional Superiority of the Left Hemisphere.**

*Hermann Förtig, Deutsch. med. Wchnschr., 48:312, Berlin, March 10, 1922.*

A regular increased size of the left lateral ventricle and left posterior horn was found in a large number of brains. It is assumed that the larger left lateral ventricle is the anatomic substratum of the functional superiority of the left hemisphere. It may also be a physiologic factor with the larger quantity of cerebrospinal fluid in the left lateral ventricle. This may be a sign of increased metabolism in the left side. The theory would be strengthened if the reverse were found in left handed persons.

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**Experimental Investigations Concerning the Course of the Oculopupillary Fibers in the Posterior Roots.**

*E. Pollak and E. Sternschein, Ztschr. f. d. ges. Neurol. u. Psychiat., 73:631, Berlin, Dec. 30, 1921.*

Unilateral severance of the posterior roots of the fifth cervical and third dorsal nerves in 2 rabbits did not result in any subsequent pupillary phenomena. This shows that the posterior roots do not exert any influence on the tonus of the *musculus dilator pupillae*. Since it is not inconceivable that individual variations might occur, the author intends to corroborate his results by a greater number of experiments.

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**Researches on the Tonic and Trophic Functions of the Sympathetic Nervous System.**

*N. Takahashi, Pflüger's Arch. f. d. ges. Physiol., 193:322, Berlin, Feb. 9, 1922.*

In order to determine the influence of the sympathetic nervous system on the development and weight of various organs, the sympathetic nerve was extirpated on one side in guinea-pigs partly in the lumbar and partly in the sacral region, and the weight of the organs on the side operated on and on the normal sides compared. The study of the blood-vessels was effected by means of radiographs taken after injection of Unna's paste. The interval between operation and killing varied from fourteen to two hundred and twenty-seven days. The one-sided extirpation of the sympathetic had no observable influence on kidneys, suprarenal glands, musculature, arteries, skeletal parts of the hindlegs or on the claws. And, *in vivo* the interference was not observed to influence the tonus of the skeletal musculature in contradistinction to the theory of the importance of the sympathetic nervous system to muscular tonus. The ovaries showed no differences. On the other hand the testicle on the operated side showed itself markedly hypoplastic though no strict relation existed to the time that had elapsed since the operation. Secondary injuries, for instance of the *vas deferens*, were excluded. Muscular tonus was tested by comparing the position of the posterior extremities when the latter were freely pendulous and also by resistance to passive flexion.

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**The Relationship between Nervous and Hormone Control of the Respiratory Center.**

*J. J. R. MacLeod and S. U. Page, Am. J. Physiol., 60:134, March 1, 1922.*

Observations were made on animals (principally cats) in which the breathing was perfectly regular one hour after decerebration by Sherrington's method. To prevent fall in body temperature the preparations were kept on a heated table with the head end somewhat raised on a hot water bag. The rectal temperature was frequently recorded. The observations included (1) the effect produced on breathing by section of the vagus nerves; (2) the relationship between the hormone and nervous control of the respiratory center; (3) the effect of vagotomy on (Sec. 1—Page 861)

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the excitability of the center toward hormones; (4) the effect of alterations in the respiratory hormones on the reflex excitability of the center; (5) the effect of injections of sodium carbonate solution; (6) the effect of injections of acid solutions; (7) the effect of breathing atmospheres rich in carbon dioxid; (8) the effect of anoxemia, and (9) the influence of section of the vagus nerve on the gradual increase in breathing which supervenes shortly after causing an animal to breathe into a closed system of tubes. Analysis of the graphic results shows that after section of the vagus nerve in decerebrate cats, the breathing usually declines somewhat in minute volume and the rate diminishes, often in some simple ratio to the normal rate. Similar section in decerebrate rabbits causes complete breakdown of the respiratory function. Increasing the percentage of carbon dioxid in the inspired air has almost exactly the same stimulating effect on respirations before and after section of the vagi, the only difference being that with high percentages of carbon dioxid, the respirations after section of the vagi become slower and the minute volume ceases to increase and may decline. The excitability of the respiratory center to afferent nerve stimulation (sciatic and vagus) was not definitely increased after the intravenous injection of fixed acid or during the hyperpnea induced by respiration atmospheres rich in carbon dioxid or poor in oxygen. Conversely it is not decreased after the injection of sufficient amounts of sodium carbonate to lower the H-ion concentration of the blood. These results show that the reflex excitability of the respiratory center is not altered by changes in the respiratory hormone (CH and CO<sub>2</sub> tension) of the arterial blood. The gradual increase in breathing, which occurs immediately after connecting the trachea with a closed system of the wide bore tubes, still occurs, it was observed, after section of the vagi:

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**A Respiratory Acceleration Phenomenon.**

*Th. Wassenaar, M. J. South Africa, 17:138, Johannesburg, Feb., 1922.*

Under profound anesthesia, the carotid arteries of a cat were ligated and tracheotomy was performed. The cat was decerebrated and after being laid back on the warmed operating table, left quiet for fifteen minutes in order that the anesthetic effect might pass off. Compression was then performed, either by gripping the thorax from the ventral side between the thumb and the other fingers and then squeezing softly, or by pressing with the flat hand on the upper side of the chest. Tracings of the respiration were recorded on a kymographion. The immediate response to the compression evoked the suspicion that the reaction was a reflex, and made it improbable that the ventilation of the lungs or even the blood circulation had anything to do with it. A special tracing of the blood pressure showed a slight fall at the commencement of compression and a quick rise after release, without either acceleration or inhibition of the heart. Shortly after decerebration, the respiration is usually decreased by compression, which seemed to indicate a reflex nervous regulation of the phenomenon. Cutting of one vagus did not destroy the accelerating effect on the respiration of compression of the thorax. When the second vagus also was cut, the respiration became very slow and sometimes stopped altogether. Stimulation of the

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skin did not alter the breathing. Pressure on the diaphragm through a small opening in the abdominal wall did not show any particular influence; the same was true of lifting of the chest wall by a thread run round a rib. Dorsoventral compression of the thorax, and sometimes compression of the abdomen, also gave the acceleration phenomenon. Raising and lowering the pressure in the pleural cavity, by blowing in or drawing out air through a cannula in the chest wall, showed that at an intermediate pressure the respiration was quickest. Stimulation of the cross-section of the midbrain, for example by lifting the cotton which covered it, destroyed the diminution of the respiratory rhythm. The whole phenomenon was possibly the result of really two opposing influences, accelerator and inhibitory, the inhibitory dominating immediately after the decerebration, the accelerator gradually taking the field afterwards. In one case the transition could be easily followed on the tracing. There was an intermediate period when the compression did not alter the breathing.

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**The Respiratory Gas Metabolism in Health and in Disease.**

*O. Rolly, Ztschr. f. d. ges. exper. Med., 26:69, Berlin, Jan. 20, 1922.*

Does a preliminary monotonous diet influence metabolism during fasting and starvation? In order to have comparative values in experiments on gas metabolism, it is first of all necessary to determine the so-called metabolism, by which may be understood the amounts of O and CO<sub>2</sub> which a fasting organism consumes and exhales per minute during absolute rest. At a certain time after the ingestion of food, all food stuffs have undergone combustion and the body will arrive at its basal metabolism. The titer of gas metabolism at that stage is the fasting titer. Twenty-four hours after the ingestion of the last food, the body is in the fasting state. The respiratory quotient during this stage is usually 0.8. Rolly kept dogs without food for sixteen days; at the end of that period one was fed only beef (albumin dog), another only rice, and a third only bacon. These tests were continued four hours or longer.

The albumin dog, in a starvation period following a mixed diet, had a respiratory quotient of 0.716. During the subsequent period of meat diet the respiratory quotient rose to 0.740, and was somewhat higher during the second starvation period. The dog fed on rice showed a respiratory quotient of approximately 1.00; it fell to 0.71 on the third day of the subsequent starvation period. In the dog fed solely on bacon, the respiratory quotient fluctuated between 0.70 and 0.77, and suffered little change during the second period of starvation.

Thus there was actually a high respiratory quotient in the dog fed with rice; this, however, was not an accommodation, since all 3 dogs showed practically the same respiratory quotient after a few days during a period of starvation following the different diets. That is, after carbohydrate food, the respiratory quotient in the fasting stage may approach the theoretic carbohydrate quotient. The same is true for albumin and fat feeding. When fasting is prolonged, however, the respiratory quotient no longer is influenced by the nature of the food ingested more than twenty-four hours previously.

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**The Effect of Intravenous Injection of Hypertonic Solutions of Various Sugars upon the Respiratory Gaseous Exchange in the Dog.**

*Max Bürger, Biochem. Ztschr., 124:2, Berlin, Nov. 15, 1921.*

By the study of the effect of intravenous injections of hypertonic sugar solutions it was attempted to prove whether under similar experimental conditions a regular temporal course in the change of the respiratory quotient and of the production of calories is recognizable after intravenous injections of sugars, also whether the disturbance of the osmotic equilibrium in itself resulted in an increased production of calories, and finally, whether the gaseous exchange after intravenous injections of convertible sugar solutions also changes when hunger and muscular work respectively precede the infusion and the glycogen depots were extensively depleted. The experiments were done on tracheotomized dogs; the sugar solutions were always of 50% strength and injected into the jugular vein; the gas analyses were conducted in Haldane's apparatus. The amount of ventilation was determined, the body temperature was tested and the respiratory tests were conducted in the Zuntz-Geppert apparatus. The values for carbonic acid production and of the consumption of oxygen were always reduced to 760 mm. pressure and to 0° C. The almost complete unanimity of the results obtained with the Zuntz-Geppert apparatus and those obtained with the chamber test were experimentally determined. The experiments with sugar injections were made with dextrose, levulose, lactose and with saccharose. The experiments show that both the dextrose and levulose entered the combustion with an increased production of total heat. The percentage of the carbonic acid in the expiratory air rises immediately after the injection of hypertonic dextrose solution and the respiratory quotient is increased from 0.703 to 0.946; at the same time the total production of heat is increased. The relative as well as the absolute values of carbonic acid are far greater after the injection of levulose than after that of dextrose. This rapid increase of the respiratory quotient and of the production of calories following the injection of levulose into the circulation indicates that this variety of sugar is directly attacked by the organism without its previous change into glycogen. This unique quality of levulose in metabolism, i.e., the greater production of calories after the injection of levulose than after that of dextrose, for a long time known by the clinician, has been recently confirmed by experiments.

After the injection of equal amounts of hypertonic saccharose and lactose solutions into the circulation, the production of carbonic acid and the consumption of oxygen are simultaneously increased and the increased production of calories is associated with a parallel rise of the respiratory quotient, but these values are in no case so high as those following the injection of dextrose and levulose respectively. This rise after the injections of saccharose and lactose should be considered as an indirect osmotic effect of the injection of hypertonic solutions and should be explained as a result of the increased cardiac and renal activities from the inrush of tissue juices into the circulation. In regard to the effect of intravenous injections of dextrose after previous periods of starvation and work, the experiments showed that the previous withdrawal of food and exhausting work does not protect the intravenously

injected dextrose from combustion in amounts of 0.5 gm. per kilo body weight. This is shown by the fact that the respiratory quotient rises from the extremely low values, such as are found after exhaustive work together with the withdrawal of food, to values of almost 1.0. Therefore the combustion of dextrose is drawn upon not only to cover the caloric necessity, but after the emptying of the glycogen depots there results a direct luxurious production of calories.

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**Is There Any Genetic Relationship between the Oxygen of Inspiration and the Acid of Carbonic Acid of Expiration?**

*Torsten Thunberg, Hygiea, 84:167, Stockholm, March 16, 1922.*

According to the author's experiments and theoretic considerations, oxygen is used in the organism to oxidize the hydrogen which exists in an active form, thanks to the hydrogen-carrying ferments (so called hydrogen-transportases). The oxygen of inspiration is, therefore, transformed into water. Hydrogen peroxid is formed, but in this, half of the oxygen remains unemployed. A catalase which decomposes hydrogen peroxid sets oxygen free so that it may be employed again as a hydrogen-acceptor. The acid of carbonic acid is represented by the acids of the molecules of food; this acid attached to carbon (in the carbon chain) is set free when water is taken away from the molecules by the action of dehydrating ferments (so-called dehydrogenases). The author's opinion that oxygen is used to form water in the process of combustion, and that the acid of carbonic acid originates from the food-stuffs or from introduced water, is corroborated by the fact that Dixon (1886) proved that water takes part in the common combustion to carbon dioxid.

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**The General Mechanism of Respiratory Movement.**

*H. Gertz, Acta med. Scandinav., 56:71, no. 1, Stockholm, 1922.*

During respiration, the form of the chest and volume of contained air undergo elastic alterations. The motor innervation producing these changes depends on variations in the chest capacity. A purely mathematical consideration of these relations, as occurring in normal respiration, indicates that the motor innervation remains inspiratory throughout the greater part of expiration and probably even to its close. The same principle holds good for all respiration, provided it be not too deep.

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**Internal Secretion and Regulation of Body Heat.**

*R. Isenschmid, Med. Klin., 18: 215, Berlin, Feb. 16, 1922.*

One distinguishes chemical and physical regulation of warmth and it is also known that the processes of warmth regulation are commanded by the central nervous system. There is not so much knowledge concerning the organs in which the regulating increase and decrease of warmth formation take place; it can be said, however, that, for quantitative reasons, the muscles and the large glands of the abdomen must play a part. But very little is known concerning the relations of the nervous centers and paths (acting in the warmth regulation) to the  
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secretory organs. A priori, there are various opinions as to the rôle of the glands of internal secretion. As the influence of the thyroid gland upon the metabolism is well known, there is a natural tendency to explain its participation in the regulation of warmth by crediting it with an influence exerted upon the chemical regulation of warmth. The activity of the thyroid increases the metabolism and, in that way, the formation of warmth in mammals. Its absence diminishes to a great extent the metabolism and the formation of warmth. The descriptions of Boldyreff have shown that animals without thyroid gland and without epithelial corpuscles have a worse physical regulation than normal animals; that is to say: in animals deprived of their thyroid gland the skin did not become warmer as did that of normal animals, the blood-vessels of their skin did not become dilated, in a regulating action, under the influence of warmer surroundings.

Recently, Mansfeld and Pape observed facts which throw a new light upon the importance of the internal secretion of the thyroid gland. The experiments made on rabbits by these authors, show that the metabolism in the regulation of warmth, at least in the heart, is not directly submitted to the influence of the centers of warmth regulation and that the regulation takes place by means of another factor, probably a chemical one. The investigators were able to prove that hypothesis, as they could demonstrate that the serum regulates the sugar consumption of the surviving heart as required for the regulation of warmth. In rabbits deprived of their thyroid gland neither warming nor cooling has any influence upon the consumption of sugar in the surviving heart. If these observations are correct they prove that the central nervous system influences, by the hormonal by-path and not directly, the organs in which the variations of combustion take place for the sake of warmth-regulation. If the facts hitherto observed are correct one must expect to find the absence of the thyroid gland manifesting itself even in the simple examination of the power of warmth regulation. The author has made experiments to determine whether rabbits deprived of thyroid could maintain, as normal rabbits do, their body temperature when the temperature of the air is modified. It was found that animals without thyroid are not much disturbed in their regulation of warmth. In more refined experiments the medulla of rabbits was divided at the level of the upper dorsal segment, kept in various temperatures, and the regulation of warmth examined for a period of several days. The reaction was far stronger than in animals with normal nervous system. Therefore it is concluded that in these animals the chemical regulation of warmth has been considerably impaired by the absence of the thyroid. The thyroid gland does not appear to be deprived of its part in the regulation of warmth, but other organs may possibly take up its function and compensate for its suppression. One sees then that regulation of warmth is an extremely complicated process.      *(To be concluded)*

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Studies on the Effect of Diet on the Weight of the Hypophysis and Thyroid Gland of the Albino Rat, and on the Action of Their Extracts on the Isolated Small Intestine.

*Lyda May Degener, Am. J. Physiol., 60:107, March 1, 1922.*  
This research was undertaken to determine whether different diets  
(Sec. 1—Page 866)

could produce alterations in weight of the thyroid and hypophysis and in the effects of their extracts on the isolated intestine. Feeding experiments with 5 diets were conducted on 200 albino rats, ranging in age from 27 to 250 days and fed for periods from 10 to 175 days upon (a) oatmeal and milk, (b) vegetables, (c) meat, (d) standard diet with potassium iodid, and (e) standard diet with thyroxin. Observations were made on the effect of each diet on (a) body weight, (b) weight of the thyroid and hypophysis, and (c) the physiologic effect of the gland extracts on the isolated intestine. In addition, the action of the extracts of the parts of the hypophysis on the isolated intestine was determined, and the effect of the diets on the weight and water content of the brain noted. It was found that the body weights in all the groups were low for the age in both control and test animals. The controls were on the average heavier by 5 gm. When compared with standard tables, the weight of all the glands was low for the body weight. Taking the averages, and recording the difference of the tests from the controls, the oatmeal thyroids were heavier than the controls by 1 mg., the hypophysis by 2 mg. In the vegetable group, the thyroid was heavier by 4 mg. The hypophysis was lighter by 1 mg. In the meat group the weight of the thyroid was somewhat greater, but that of the hypophysis was not altered. In the potassium iodid and thyroxin groups there was practically no modification in the weight of the test glands. Concerning the activity of the gland extracts, the author observed for the thyroid no definite difference in the effects of the control and test extracts in any of the diet groups. In the case of the hypophysis the test extract caused a contraction of the intestinal strip (in the oatmeal and the vegetable diet groups). The control extract always caused relaxation. The responses to the extracts from the nervous and glandular lobes of the hypophysis were found to be opposed to each other. The glandular lobe extract caused contraction and the nervous lobe extract relaxation. The several diets did not modify the weight of the brain. The percentage of water in the brains of the test and control series was found to agree perfectly.

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**Influence of the Hypophysis on Growth.**

*B. A. Houssay and E. Hug, Rev. Asoc. médica argentina (Biol. Sect.), 34:269, Buenos Aires, Nov., 1921.*

Houssay's and Hug's experiments were mainly on young dogs. The results do not establish the influence of the gland as a factor essential to growth. After extirpation of the hypophysis symptoms appeared, such as tachycardia, increased temperature, and abundant elimination of nitrogen, urea chlorids and phosphates, but these symptoms were never constant. Polyuria appeared frequently, oliguria rarely. Glycosuria was commonly observed. The most important modification was the arrest or retardation of growth, which manifested itself from one to two and one-half months after operation. In some instances the animals retained all the characteristics of the infantile stage. Some grew normally; in these cases fragments of the gland persisted. But in others only insignificant traces of the intermediate portion were found. In other cases, with very marked retardation in growth, extensive rests

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of gland from one-fifth to one-third, or of the anterior lobe and the intermediate portion, remained. This disagreement in results indicates: (1) This gland is not an essential factor to growth; or (2) the functional importance of the remaining portions is variable; or (3) these symptoms are due to the infundibular lesion and are of nervous origin. In most cases at least a vestige of the gland persisted. The degree of the dystrophy (general retardation of growth, delayed calcification of the teeth, adiposity, atrophy of the tail, thyroid changes, genital hypoplasia, infantile blood-picture) depended upon the amount of the gland remaining. The crucial point to be determined is whether these symptoms indicate glandular insufficiency or dystrophy of the nervous system.

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**The Hypophysis and the Metabolism of the Carbohydrates.**

*B. A. Houssay, E. Hug and T. Malamud, Rev. Asoc. méd. argentina (Biol. Sect.), 34:290, Buenos Aires, Nov., 1921.*

This communication relates the results of several investigations performed on dogs from 1908 to 1921. Glycosuria was frequently observed during the first days after extirpation of the hypophysis or following a lesion of the cerebral zones in the vicinity. These dogs generally exhibited a normal tolerance for sugar administered by mouth. Some dogs with dystrophia adiposogenitalis presented greatly increased, which later returned to a normal value. Glucose injected intravenously produced the same tolerance. Following the extirpation of the hypophysis there was no increase in the tolerance.

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**Urine and Blood of Dogs Following Extirpation of the Hypophysis.**

*B. A. Houssay and P. Mazzocco, Rev. Asoc. méd. argentina (Biol. Sect.), 34:327, Buenos Aires, Nov., 1921.*

A study was made of the composition of the blood and urine of hypophysectomized dogs, of controls operated on without extirpation of the gland, and of normal controls. All the animals were kept under the same conditions and given similar food. Their urine was tested for urea, chlorid, creatinin, and total nitrogen. No differences were observed in the quantity, density or constituents of the urine of test animals and of controls.

Blood was drawn from the femoral artery of the dogs, rapidly and without anesthesia, and tested by the method of Folin and Wu. The blood of the hypophysectomized and of the control animals revealed no changes, as regards the nonprotein nitrogen, chlorid, glucose, creatinin, and total creatinin content. The calcium content was decreased in the hypophysectomized dogs, but no certain conclusion can be drawn, as the quantity of this substance varies in the blood of normal dogs.

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**The Function of the Chromaphil Tissues in Relation to Splanchnic Stimulation.**

*A. W. Sheen and Swale Vincent, Brit. M. J., London, March 4, 1922, p. 343.*

Experiments on dogs, cats and rabbits show that peripheral splanchnic (Sec. 1—Page 868)

nic stimulation produces a characteristic curve in which an initial rise is followed by a marked dip and a prolonged secondary rise. Elimination of the adrenals from the circulation abolishes or reduces the dip, the more usual effect of splanchnic stimulation being a simple prolonged rise. Some investigators maintain that there is a difference in reaction between dogs and cats; in the former the dip and secondary rise are abolished after adrenal elimination, but in the latter, elimination makes no difference in the curve. Experiments conducted by the authors on cats show that by any method of adrenal elimination the normal curve is seriously altered; the dip is frequently abolished, and is always considerably reduced; a small dip sometimes persists after total elimination of the adrenals. The dip, in part at all events, is probably due to liberation of adrenin into the blood through vasoconstrictor impulses reaching the adrenals and causing them to contract, the small amount liberated having a vasodilator effect on the peripheral arterioles. This effect is temporary, the rise being again produced and maintained as long as stimulation lasts. While the adrenal elimination is probably an important factor in altering the curve, further experiments are required to determine completely the origin of the dip. Since some dip may occur after adrenal elimination, a part of the effect must be normally due to influences other than chromophil secretion.

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**Comparative Importance of the Cortical and Medullary Portions of the Suprarenal Capsule.**

*B. A. Houssay and J. T. Lewis, Rev. Asoc. médica argentina, (Biol. Sect.), 34:254, Buenos Aires, Nov., 1921.*

Houssay and Lewis discuss which of the 2 portions of the suprarenal is of vital importance, and refer to previous work and to the varying conclusions as to their relative importance. The authors performed experiments on 16 dogs; the left capsule was reached by the lumbar route and drawn out through the opening; an incision was made along the edge, and the entire medullary portion—which is easy to differentiate, as it is more friable than the cortex—was curetted. To insure total extirpation, part of the cortex should be removed. Bleeding is slight, and ceases spontaneously. Both borders of capsule were sutured. After ten or fifteen days the right capsule was extirpated.

Three animals died within forty-eight hours. One was in complete health five days after intervention. Two were allowed to live and, after two months, seemed to be in a normal condition. The rest were operated on at various periods. Bilaterally decapsulated dogs died in every instance fifteen to fifty hours after operation.

The cortex, in the dogs which died prematurely, was greatly altered, being practically absent in one case, so that an almost complete decapsulation was observed. Histologic examinations were made of those which survived for the longest time; serial sections were made of the capsule. In one case only traces of medulla were found. The cortical cells were normal; a great number of protoplasmic inclusions and typical spongy tissue were found in places. Sclerotic bands covering almost all the cortical portion radiated from the scar in the center of the capsule.

Cristiani's investigations on rats cannot be considered conclusive, on account of the tolerance of rats for total decapsulation; 60-80% survive operation.

Vassale and Zanfognini obtained results opposite to these; their negative findings have no value as against the positive facts proven by these observations, as the death of the animals may have been caused by secondary lesions not situated in the capsule.

The following facts prevail: (1) Extirpation of both capsules is fatal. (2) Extirpation of the chromaffin substance of both capsules does not interfere with life. This proves that the cortical portion is the vital part, although it cannot be affirmed that the medullary portion is not important.

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#### The Vascular Relations of the Suprarenals as Affecting the Secretion of Adrenalin.

*E. Gley and A. Quinquaud, J. de physiol. et de pathol. gén., 19:504, no. 4, Paris, 1922.*

Ligation of the suprarenal venous trunks has been considered equivalent to ablation of the glands. On account of the possibility that anastomoses of the vessels might permit adrenalin to reach the general circulation in spite of ligation, Gley and Quinquaud have made a special study of the question. It is found that there may be anastomoses between the suprarenal venous trunk and the perirenal plexus. Such anastomoses are rare and relatively unimportant. Ligation is usually effective, and stimulation of the splanchnic nerve produces its usual results. In view of the possibility that anastomoses may exist, ablation of the suprarenals more surely eliminates the influence of adrenalin than is the case in ligation of the venous trunks.

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#### Effect of the Thyroid on Metabolism with Special Reference to Temperature.

*Paul Schenk, Arch. f. Exper. Path. u. Pharmol., 92:1, Leipzig, Feb. 28, 1922.*

Metabolism experiments were performed on rabbits who had been fed with oats. The experiments lasted twenty-four hours during which time the animals were given nothing but water. After determining the respiratory quotient, thyroidectomy was done or the activity of the thyroid was stimulated by the application of cold and ether.

The fasting animal had a respiratory quotient of 0.7, which fell from day to day, chiefly because of oxidation of fat, and rose on increased catabolism of albumin to 0.8 (increase of nitrogen in urine). In the fasting thyroidectomized animal there was a slight fall in albumin consumption, and a pronounced fall in calcium excretion, the respiratory quotient reaching values of from 0.5 to 0.4 on the fifth or sixth day. The premortal increase in albumin metabolism was almost completely lacking. In analogy with these results, an increase in metabolism was brought about by the administration of thyroid preparation (thyroglandol, which was almost entirely free from nitrogen and contained only iodin). This was given by intravenous injection.

In normal animals there was only an increase in nitrogen excretion, while in thyroidectomized animals the nitrogen excretion and respiratory quotient rose temporarily. From these experiments, the author concludes that the hormone of the thyroid is an amid-like catabolized albuminoid, for the catabolism and effectiveness of which traces of iodin are necessary.

As to the relation between the thyroid and temperature it was found: (1) When normal animals are suddenly exposed to cold more thyroid hormone passes into the circulation, and during the return to normal temperature there is a rise of  $\text{CO}_2$  and  $\text{O}_2$ , as there is in thyroidectomized animals after the injection of thyroglandol. (2) In thyroidectomized animals the return to normal temperature is much slower than in normal animals. (3) Injection of serum from a normal animal, that has been exposed to extreme cold, into a thyroidectomized animal, increases the process of oxidation in the latter from 40 to 50%. Normal serum injected into a nonthyroidectomized animal has almost no effect on the respiratory quotient, and the serum of a thyroidectomized animal is just as ineffective when injected into another thyroidectomized animal. The reflex of chemical heat regulation is as follows: Heat center to sympathetic to stellate ganglion to thyroid. The latter gives off a hormone which is carried by the blood to the cells, and furnishes the stimulus to increased heat production.

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## 1b. BIOLOGIC AND ORGANIC CHEMISTRY

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### Refractometric Analysis.

*Jan Becke, Časop. lék. česk., 61:161, Prague, Feb. 25, 1922.*

Chemico-analytic methods must be used in the study of metabolism of the body. These are believed to be rapid and easy to carry out but the chief requirement is that they be correct and constant and that the methods be applicable to the smallest quantities. The methods based on a determination of the refraction of solutions meet these conditions. The Tauch refractometer with the prisms is of great value. It is possible to determine the refraction of 0.05 c.c. solution within limits of 1.32540 and 1.36667. The quantity of the chief ingredients may be determined by refraction if the substance is a solution with a constant relation.

The method of de Crinis which makes use of the refractometer for precipitation analyses of reagents of the same weight has been extended by the author to include precipitation caused by chemico-analytic conditions in which precipitation of similar weights can be made only exceptionally.

Relative refraction is obtained by subtracting the refraction of water from the refraction of the solution. The relative refraction of the pure solution is the product of the weight per cent. of the dissolved substance and the relative refraction of the 1% solution of the same substance at  $17.5^{\circ}\text{ C}$ . The mixture of 2 equal weights of 2 solutions which do not react on one another results in a refraction which is equal to an arithmatic average of the original refraction. The resulting refraction is less than the one calculated if (Sec. 1—Page 871)

the 2 solutions react (because of the precipitation of one of the substances). This diminution is proportional to the quantity of the precipitated substance. Refraction is also an additive peculiarity of the solutions and is proportional to the quantity of the dissolved substances. The difference between the calculated and the found refraction is in direct relation to the resulting concentration of the substance if there is a reaction between the mixed solutions in which certain of the ingredients are precipitated. This method allows the analysis of solutions of sulphate containing 0.02—1.0% SO<sub>3</sub> if the precipitation is made with an N/10 barium chlorid solution with a  $\frac{1}{2}$  excess. It is suitable for the determination of sulphates, ether sulphates and chlorids in the urine.

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#### Potential Acidity in Colloidal Complexes of Living Organisms and Its Activation Through Certain Physical Forces.

*Alberto Scala, Ann. d'igiene, 31:743, Rome, Dec., 1921.*

Some time ago it was observed that if vegetable tissues cut into very thin slices were washed for a long time in a great quantity of distilled water and the degree of acidity or alkalinity of the wash water, concentrated at about 70° C. in a hot water bath, was determined, a strange fact appeared. In the first washings acid was eliminated, and in the succeeding washings alkali was eliminated. If the vegetable tissues, immersed in distilled water, were then heated, at the moment in which free alkali was eliminated, beyond 20°, there was an immediate inversion of the reaction, which from being alkaline became acid. The acidity increased with the heat up to the point of 60° and then it decreased as the temperature rose to 100°. Hence, the combined salts in the colloidal complexes of the vegetable tissues are not eliminated by entire molecules, but by alternating hydrolyzed ions. With cold washings, this elimination reaches a limit in which an equilibrium is established between the two activities of hydrolysis, so as to make it appear that the ions combined with the colloids are entirely eliminated. The experiment of heating described above proves that this is not so, and that there still exist a potential acid energy and a potential alkaline energy which may become active if external forces enter to disturb the equilibrium of the complexes. These investigations have been repeated and completed. It has thus been observed that in the leaves of almost all vegetables which upon second washing yield free alkali, such elimination ceases and is substituted by that of acid as soon as the temperature of the immersion water reaches 30°; up to 60° the acidity increases and then, up to 100°, decreases. This acidity which appears as a result of heating is called potential acidity. It comes from mineral ions with negative electric sign, united to the complexes with an affinity such as to render hydrolysis impossible at ordinary temperature, while it is possible with higher temperatures. Experiments executed upon animal substances (flesh, blood) have demonstrated that the composition of colloids with mineral salts is identical in the vegetable and animal kingdoms: in the case of the latter, there appears an unsuspected acidity just at the moment in which alkali is yielded in discrete quantity. It is true, however, that animal substances show a very high degree of acidity at the beginning which persists through prolonged washings, while vegetable substances yield free alkali after very few washings. It is probable that in life

the muscles have an amphoteric or slightly acid reaction, and that, through the great psychic shock of death, there takes place a decomposition of acid producing colloidal complexes; hence the marked acidity met with in washings of animal substances. This effect of psychic shocks explains those cases in which keen displeasure, sudden joy, or great fear causes disturbances or illness.

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**The Actual Reaction of the Cerebrospinal Fluid.**

*Klothilde Meier, Biochem. Ztschr., 124:137, Berlin, Nov. 21, 1921.*

The actual reaction of the cerebrospinal fluid, that is the concentration in free hydrogen ions, has heretofore been considered as considerably more alkaline than that of blood. As the carbonic acid is an important factor in the reaction of body fluids, its escape must be prevented during both the withdrawal and the examination of the fluids. This was accomplished by the manner of withdrawal. The hydrogen value was determined by the indicator method advanced by Friedenthal, and also by gas analysis with the use of the Bancroft differential apparatus. In the colorimetric method, neutral red was added as an indicator with a pipette and the color was compared with a solution made of copper phosphate solution of known hydrogen value. After the determination of the original carbonic acid volume percentage—hereafter known as actual carbonic acid content—the curve of carbonic acid combination was determined by titration of the spinal fluid with carbonic acid according to the method of Straub and Meier. If the curve acquired in this way with the carbonic acid tension is used as abscissa and the volume percentage as ordinate, the natural actual carbonic acid tension of the cerebrospinal fluid can be obtained from the primordial content of the original fluid and from the combining curve. The calculation of the hydrogen figure proceeds, as in the blood, from the carbonic acid tension and carbonic acid content according to the formula of von Haselbalch.

On examining the cerebrospinal fluid of 2 absolutely healthy individuals, the hydrogen ion concentration with the indicator method showed values of 7.38 and 7.33, and by computation from the acid capacity and combination curve the value in the second case was 7.35. As pH 7.33 is assumed as the reaction of the blood, the reaction of the cerebrospinal fluid in normal cases is only slightly less alkaline than or equal to that of the blood. The total content of carbonic acid in the cerebrospinal fluid was determined as 52.8 volume per cent. in one normal case; it is approximately as great as that of the blood, as the latter, according to Straub and Meier varies between 47 and 67 volume per cent. The carbonic acid combination curve is considerably less than that of the blood and has a slightly smaller buffer reaction than that of the serum. The cerebrospinal fluid was also examined in a series of patients, including cases of tabes dorsalis, glaucoma, temporary blanching of the papilla, tuberculous meningitis and purulent meningitis, in which it was shown that tabes dorsalis shows no reaction and no change in the power of carbonic acid combination of the cerebrospinal fluid. These properties are also unchanged by the tuberculous inflammation of the meninges. In one case of purulent meningitis without bacteriologic finding, however, the carbonic acid tension and the carbonic acid com-

bining power were somewhat diminished with the normal reaction. In one case of epidemic meningitis there was acidosis in the cerebrospinal fluid, the actual reaction was reduced to 7.06 and the carbonic acid tension was increased, at one time up to 53 mm.

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**The Lipoids of the Crystalline Lens.**

*M. Goldschmidt, Biochem. Ztschr., 127:211, Berlin, Feb. 28, 1922.*

In the alteration of the human crystalline lens in senile cataract, the occurrence of cholesterol is very frequent and macroscopically easily detectable. The results of estimations are, however, not uniform and the attempt was therefore made to gain an insight into the quantitative relations with due regard to the liability of the lipoids and the difficulties resulting therefrom. For the researches, lenses of persons just previously deceased were employed. They were arranged according to the individuals' ages and kept in absolute alcohol, the latter being filtered off through a fat-free filter. The lenses were ground and dried in vacuum till constant. Extraction was carried out in Soxhlet's apparatus with alcohol, benzin, acetone and lysol. The quantitative estimations show that cholesterol is at a minimum during the second decennium and rises to the maximum during the seventh to eighth decennium. Phosphatid attains its maximum in the second decennium, namely in a period of cholesterol minimum, and diminishes toward the seventh decennium. The acetone-soluble fraction has its maximum in the second decennium while the benzol-soluble fraction finds its lowest level at this period. The biologic importance of these relations lies on the one hand in the rôle of the lipoids as oxygen fixers, and on the other in the resistance of the cell, whose electric isolation and ionic permeability seem to depend on the relation of lecithin to cholesterol.

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**On the Cleavage Products of the Crystalline Lens.**

*Yoshizumi Hijikata, J. Biol. Chem., 51:155, March, 1922.*

The results of an investigation of the cleavage products of the crystalline lens of the ox represent a contribution to the knowledge of the chemical composition of the lens tissue. Fresh material was obtained from a slaughter house and the water and ash content determined by drying to constant weight at about 105° C. Then followed hydrolysis of the lens by hydrochloric acid and fractionation of the esters of the mono-amino-acids. The hydrolysis of the lens of the ox yielded 13 cleavage products: alanin, valin, leucin, aspartic acid, glutamic acid, lysin, arginin, phenylalanin, tyrosin, prolin, tryptophan, histidin, and adenin.

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**The Chemistry of the Lung. I.**

*Ubaldo Sammartino, Biochem. Ztschr., 124:234, Berlin, Nov. 21, 1921.*

An attempt was made to obtain a picture of the complete chemical constitution of the lung. The difficulties lie in the fact that the organ  
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contains not only its own tissue structures, but blood and lymph, the washing out of which is capable of carrying away substances from the tissues to be examined. For this reason it is necessary to examine a freshly exsanguinated lung. The lipoid bodies of the cattle lung were first examined; the same method was applied as in the brain except for slight changes, because the lung contains chlosterin and cholesterin ester in addition to glycerin fats. The cattle lungs, after exsanguination, were dried in a vacuum apparatus and the powder was exhaustively extracted with benzin; the benzin extract was worked up by itself after concentration in a vacuum; the lung powder exhausted with benzin was then saturated with alcohol; the alcoholic extracts were combined and concentrated; and the residual powder was cooked with water and the extract was concentrated; the benzin extract was precipitated with acetone and extracted with ether; the cephalin was precipitated from the ethereal solution by alcohol; the acetone fraction and also the white matter, the so-called protagon, were then worked up.

The examination showed that the lung tissue contains considerable amounts of free cholesterin, cholesterin esters, glycerin palmitate and unsaturated phosphatids (lecithin and cephalin), also large amounts of cerebrosids and phosphosulphatids. The amount of the unsaturated phosphatids is slight in comparison to that of the protagon, a mixture of cerebrosids and phosphosulphatids. The abundance of cholesterin and cholesterin esters is striking.

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**The Hydrogen-Ion Concentration of the Intestinal Contents.**

*Seizaburo Okada and Minoru Arai, J. Biol. Chem., 51:135, March, 1922.*

The authors examined electrometrically the duodenal contents of various hospital patients, removed with an Einhorn duodenal tube under various conditions. The tabulated results show a variation from pH 4.80 to 7.97. The duodenal and ileal contents of 5 dogs were examined from one to three hours after a meal consisting of 1 lb. meat. The tabulated results show a variation from pH 6.15 to 7.83.

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**Method for Determining the Presence of Chlorin in the Tissues.**

*O. M. Pico and J. J. Murtagh, Rev. Asoc. méd. argentina (Biol. Sect.), 34:286, Buenos Aires, Nov., 1921.*

Pico and Murtagh describe a new method for the determination of chlorin in small fragments of organs. By this easy and rapid method the proteins are precipitated with phosphotungstic acid, following disintegration of the tissue with a concentrated solution of caustic soda and subsequent acidification.

Three grams of issue are placed in a small Erlenmeyer tube with 5 cc. of a 40% solution of caustic soda, which is heated and slightly stirred until disintegration is complete. When this is cooled, 7 c.c. of concentrated nitric acid solution are added drop by drop; this is stirred and cooled under a cold water faucet. A liquid of great acidity is thus

obtained for the coagulation of proteins. To this liquid an equal volume of phosphotungstic acid, 10% solution is added, after waiting a few minutes until coagulation is complete and it is integrated by the chlorin titrate. To produce titration, 4 c.c. of indicator, (solution of starch, citrate, nitrite) are added drop by drop to the solution of IK; a blue color appears promptly and does not disappear on shaking, even after some time. This completes the test.

The authors' results (as shown in a table) correspond very closely to those of Austin-Van Slyke.

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**The Effect of Loss of Carbon Dioxid on the Hydrogen-Ion Concentration of Urine.**

*E. K. Marshall, Jr., J. Biol. Chem., 51: 3, March, 1922.*

Few determinations of the carbon dioxid content of urine have been made, and for those that have been made no special precautions were taken by the investigators to avoid loss of carbon dioxid during voiding. Marshall determined the carbon dioxid content of urine by means of the Van Slyke apparatus using 0.5-5 c.c. of urine depending on the concentration present. A double extraction was always made and the carbon dioxid was absorbed with alkali. The total carbon dioxid (free and combined) was then calculated from the volumes of gas obtained. The hydrogen-ion concentrations were determined by means of Henderson and Palmer's method with modifications in the choice of indicators and amounts of urine used. Frequently the determinations were made on the undiluted urine and were occasionally made under oil to prevent any possible escape of carbon dioxid. All the specimens were obtained from normal men who voided into a narrow cylinder with as little dropping of the stream through air as possible. A sample for the carbon dioxid was transferred to the apparatus in less than one minute. The hydrogen-ion concentration was also determined at once. An estimate of the amount of the loss of carbon dioxid in using this procedure was obtained as follows: A sample of urine was collected without exposure to air by a method similar to that used by Frederick and another sample was obtained at the same time by voiding into a cylinder or by allowing the urine obtained without exposure to air to run through air. The carbon dioxid and hydrogen-ion concentration were determined in each as quickly as possible. The tabulated results show that the loss by the method used is less than 10%. The magnitude of the error which may be caused by the escape of carbon dioxid from urine in the determination of the hydrogen-ion concentration is shown by the author in one of the tables in the article. Urine samples were collected and the pH determined at once. A sample (5 to 10 c.c.) was then poured into a 250 c.c. Pyrex flask and shaken for one minute, and the pH again determined. This was judged to represent roughly the agitation of samples which might take place where no precautions were taken. Determinations are also included in the tabulated data of samples shaken for ten minutes. The more alkaline specimens were obtained after the ingestion of 3 to 10 gm. of sodium carbonate. The results show that the effect of loss of carbon dioxid on the hydrogen-ion concentration is very slight in the case of acid urines. In some cases the effect is quite pronounced and in such cases it was observed

that the urine was very dilute. In a number of the cases recorded in the table it was found that ten minutes' shaking removed practically all of the carbon dioxid originally present (or the carbon dioxid tension was approximately that of atmospheric air). Change of reaction was prevented in a concentrated urine by the efficient concentration of the buffers present. In dilute urines the efficiency of the phosphates as buffers is decreased because it has been shown that water diuresis causes only a slight increase in the total amount of phosphate elimination, while the carbonate is markedly increased in absolute amount and generally in percentage. An examination of the neutral or alkaline urines obtained after the administration of sodium bicarbonate indicates that the error due to the escape of carbon dioxid is very great. Even after ten minutes' shaking, only a small part of the carbon dioxid is removed from the more alkaline urines. The final hydrogen-ion concentration when equilibrium is established will depend, of course, on the original concentration of bicarbonate. In these urines of high bicarbonate content, the other buffers (phosphates) are in insufficient concentration to prevent change of reaction, when carbon dioxid is allowed to escape.

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**A Method for the Estimation of Total Base in Urine.**

*Cyrus H. Fiske, J. Biol. Chem., 51:55, March, 1922.*

This method, up to the final step in the analysis, is merely an adaptation of long used schemes for the separation of the bases sodium, potassium, calcium and magnesium from other substances in urine. The urine, after being washed with sulphuric acid and nitric acid, is treated with ferric chlorid to remove the phosphate, and with ammonium acetate to remove the excess iron (as the basic acetate). The filtrate from these operations contains the bases, which are finally obtained as sulphates, free from interfering substances, by ignition with sulphuric acid and then with ammonium carbonate. The final residue is analyzed for sulphate by the benzidin method, and the total quantity of 0.1 N base present calculated from the results of this analysis.

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**Carbonic Acid and Bicarbonate in Urine.**

*James L. Gamble, J. Biol. Chem., 51:295, March, 1922.*

Measurements of pH and of the concentrations of free and bound carbonic acid in a series of 55 urine specimens collected in such a manner as to prevent as nearly as possible loss of carbon dioxid, permit the author to make the following statements: Free carbonic acid in urine has a nearly stationary value. The bicarbonate content of urine varies inversely with the urinary pH. In consequence of the nearly stationary value for the numerator of the ratio of  $H_2CO_3$  to  $BHCO_3$ , where "B" represents a univalent atom of base, the bicarbonate content of urine at a given pH is an approximately constant value. The total carbonic acid content of urine (free plus bound) falls rapidly with increase in pH, owing to the diminution of bicarbonate which accompanies rise in pH. These findings permit the inference that the elimination of carbonic acid in urine is determined by the carbon dioxid tension of blood plasma. Maintenance in the urine of an ap-

proximately constant concentration of free carbonic acid greatly limits the alkaline shift in the reaction of urine following increase in base elimination. The reaction of urine of a pH below 7.0 is much more a function of the carbonic acid-bicarbonate ratio than of the ratio of the phosphates. The reaction of voided urine may, therefore, rapidly increase in alkalinity because of loss of free carbonic acid, unless collected with precaution against loss.

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**The Detection of Acetaldehyd in Urine.**

*Wilhelm Stepp, Biochem. Ztschr., 127:13, Berlin, Feb. 28, 1922.*

Since acetaldehyd was found in the blood and urine of diabetic patients, this substance has been searched for in other diseases. But as ketones and aldehyds occur together and the tests in use depend on the reaction capability of the carbonyl group, methods are described that permit the certain detection of acetaldehyd as well as acetone in urine. The reactions are carried out in urine distillate; 20-40 c.c. urine are employed, acidified with acetic acid. The receiver is cooled with ice water. Reduction with ammoniacal silver solution is obtained by adding 2-3 drops Tollens' reagent to the distillate to be tested. In the presence of aldehyd, a dark color or a black precipitate, is produced after a few minutes, or on standing some time, according to the amount of aldehyd present. Warming is best avoided entirely. Tollens' test is positive even in dilutions of 1:100,000 in the course of five minutes. Formic acid reduces silver nitrate solution but not ammoniacal silver solution. Reduction of Fehling's solution takes place after standing some time and with larger amounts a dense red precipitate of cuprous oxid is formed, while small amounts give merely a pronounced green coloration. As no volatile substances except aldehyd reduce Fehling's solution in the cold the test is an important one. The red coloration with fuchsin-sulphurous acid is obtained with small amounts of aldehyd only on long standing. Acetone gives no reaction with fuchsin-sulphurous acid. Levin's modification of Rimini's test with piperidin, in place of diethylamin, is useful and is best carried out by adding sodium nitroprussid to the distillate and covering with piperidin. At the point of contact a blue ring is formed in the presence of aldehyd. This reaction is not given by formaldehyd, trichloraldehyd, isobutylaldehyd, benzaldehyd, salicylaldehyd and phenyl-acetaldehyd nor by oenanthol and furfrol. The condensation process of the acetaldehyd dimethylhydroresorcin represents a method permitting the detection of acetaldehyd in body fluids in the presence of acetone with absolute certainty. Two molecules of dimethylhydroresorcin (dimedon) with one molecule of aldehyd liberate one molecule of water and give crystallizing combinations (alkylenbisdimethyl-hydroresorcin) which are easily converted into their anhydrides, whose melting points are considerably removed from their own.

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**A Colorimetric Method for the Determination of Sugars in Normal Human Urine.**

*Otto Folin and Hilding Berglund, J. Biol. Chem., 51:209, March, 1922.*

Extensive use, by the authors, of this method has shown it to be both simple and practical. The preliminary treatment consists of merely (Sec. 1—Page 878)

shaking the urine with "Lloyd's alkaloidal reagent," a concentrated fullers' earth. This reagent removes most of the coloring matters together with the uric acid, creatin, and the creatinin, yet does not take away the the sugar. It is not necessary that every trace of creatinin should be removed, for relatively considerable amounts have absolutely no effect on the sugar method of Folin and Wu.

The process is as follows: To 5 c.c. urine add 5 c.c. tenth normal sulphuric acid and 10 c.c. water. Add 1.5 gm. Lloyd's reagent and shake gently for two minutes. Filter. Of the filtrate 2 c.c. are the usual amount used for the sugar determination. The above mentioned dilutions are for concentrated urines. With more dilute ones, take 10 or 15 c.c. and reduce the amount of water taken. The shaking with Lloyd's reagent should not be continued longer than two minutes, because the reagent is gradually dissolved by the acid, and because longer shaking does not take out any more. The colorimetric determination of the sugar in the filtrate is made in exactly the same manner as in the case of blood filtrates. For determination of the total sugar the authors hydrolyze as follows: To 10 c.c. of the filtrate obtained after shaking with Lloyd's reagent add 1 c.c. 10% HCl and heat in boiling water for seventy-five minutes. For purposes of subsequent dilution heat in test-tubes graduated at 20 c.c. After hydrolysis cool thoroughly and neutralize with normal sodium hydroxid. An indicator is not necessary, as the cloud produced from the material dissolved out of Lloyd's reagent furnishes an adequate indicator of the degree of neutrality required. Add the alkali until the cloud so formed does not disappear on shaking. Dilute the neutralized hydrolysate to the 20 c.c. mark. Add a small pinch of Lloyd's reagent and invert half a dozen times, to remove most of the coloring matter formed during the hydrolysis; 2 c.c. of this more dilute filtrate are usually a suitable amount for this determination also. The standard sugar solutions to be used are such as contain 1 and 2 mg. glucose per 10 c.c. (same as for blood.).

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**Note on the Gasometric Determination of Urea.**

*Raymond L. Stehle, J. Biol. Chem., 51:89, March, 1922.*

The author made additional analyses on pure urea and urea oxalate solutions, obtaining results which he has tabulated. In calculating the results of urea determinations by the gasometric method described by the author, a certain amount of error is involved. The solution the results of ureau determinations by the gasometric method described by the author, a certain amount of error is involved. The solution left in the apparatus at the end of a determination is a rather concentrated one and hence it is not correct to assume that its vapor tension is the same as that of water. This erroneous assumption was made in the original description of the method because vapor tension data for hypobromite solutions were unknown to the author at the time, but the error introduced is not large enough to invalidate the method for most purposes. Recently Dehn has submitted some data on this point. To make these applicable to the method it is necessary to prepare the hypobromite solution as described by Dehn with the omission of the final step, viz., doubling the volume with water. Then by using 1 c.c. of the solution to be analyzed, 1 c.c. of rinse water, and 2 c.c. of the

hypobromite solution the vapor tension of the solution in the apparatus should approximate closely the tension called for by Dehn's table. Dehn's solution is prepared by dissolving 100 gm. NaOH in 250 c.c. water, adding 10 c.c. Br to each 100 c.c., and doubling the volume with water.

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**The Hypobromite Reaction of Urea.**

*Paul Menaul, J. Biol. Chem., 51:87, March, 1922.*

In the determination of urea in the urine of experimental animals a discrepancy in the results was noted upon using the urease method of Folin and Youngburg and the hypobromite method of Stehle, the hypobromite method giving low results. Menaul says that since the reaction between sodium hypobromite and urea is nearly instantaneous, it is not clear why Stehle considers that in his method the reaction takes place in a vacuum, for it is apparent that the reaction has proceeded for some time before any vacuum can be obtained. In order to solve this question a number of determinations were made by using pure urea oxalate. The apparatus and pipette were calibrated with mercury. The hypobromite solution was added through the exit tube (Van Slyke apparatus) subjected to vacuum, the air expelled, then the urea solution and rinse water were added through the graduated cup, the air dissolved in them having been previously determined. The author gives a table of representative results obtained by following the procedure in the original article of Stehle, using also the strength of bromin recommended by Dehn and Krogh. These figures are claimed to be in accordance with the findings of Chattaway, Dowell, and Krogh, that there is not a quantitative liberation of nitrogen when urea is acted upon by hypobromite.

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**The Physicochemical Properties of the Uric Acid Colloid and of the Oversaturated Solutions of Uric Acid.**

*H. Schade, Ztschr. f. klin. Med., 93:1, Berlin, Jan. 25, 1922.*

When uric acid is precipitated from oversaturated solutions, there occurs the formation of an intermediate colloid stage. From such oversaturated solutions, all the uric acid can be obtained in the form of jellies resembling gelatin when, the reaction having been neutralized, the uric acid is precipitated very rapidly. This happens when hot solutions of urate of lithium, sodium, potassium, or ammonium contained in narrow vessels with thin walls are put into ice water.

*Properties of the uric jelly (U-jelly).* The 1% jellies are the most valuable for the study of their properties. They are tolerably soft; 5% jellies take the consistence of boiled albumin. The fresh jellies are transparent and structureless even under the most powerful microscope. Nevertheless, if the precipitation becomes slower, microscopic drops are to be found in the jelly; these drops become larger as the precipitation becomes slower and they can attain a size equal to 40 times that of a red blood corpuscle; meanwhile they remain quite transparent, without any sign of crystal formation. As the jelly becomes older it gradually loses its transparency. When it dries in the air, it slowly assumes a crystalline character. Cold favors the conservation of

the jelly; the higher the temperature, the more rapid is the shrinking and the crystalline transformation. An acid reaction corresponding to pH  $10^{-6}$  is the most favorable for the formation of the jelly. Although we have to deal with oversaturated solutions (concerning the crystalline state), the fresh U-jelly can be dissolved without any residue, by moderate heating. It can also be dissolved in water without the action of heat. This solution is dialyzable. Age diminishes to a great extent the resolubility of jellies. To this fact corresponds also the behavior of the permeability, the curve of which at first slowly sinks corresponding to the period in which the jelly remains absolutely cold; then at the moment the solution begins to become cloudy (in about one-half hour) the curve falls abruptly with a sharp angle, and later (after an hour and three-quarters or two hours), the curve is transformed into a line which does not descend again. The transformation of jellies into the crystalline stage, however, is of very long duration in spite of the rapid progress in the beginning and is arrived at only after months; it is then that the solubility attains the normal value in relation to the crystalline state.

*Forms of uric acid in the oversaturated solutions.* The formation of colloid in oversaturated uric acid solution depends strictly on determined concentrations of H-OH ions; when the oversaturation is high, we may go up to about pH  $0.5 \times 10^{-8}$  (the point at which the coloration of phenolphthalein appears); when the oversaturation is low, the neutral point must not be exceeded toward the alkaline side; but the optimum zone lies at pH  $10^{-7}$  to  $10^{-8.5}$ , that is to say, quite near the neutral point on the acid side. The following facts show that the U-colloid exists already in the oversaturated solution before the precipitation begins: (1) The appearance of opalescence, which, as the solution cools down, transforms itself into distinct colloid formation (droplets). (2) The appearance of the Tyndall-cone when the solution is illuminated with an intense source of light, long before any visible cloudiness is seen. (3) The ultramicroscope cannot prove the existence of the colloid. (4) The ultrafiltration gives not only a positive proof of such existence but also gives a quantitative measure of it. (5) The microscopic demonstration is most successful for solutions of a not very extensive degree of oversaturation, in which the best conditions exist for the development of droplets before precipitation; these solutions are those which have to be considered for therapeutic use. Freshly prepared oversaturations are in the stage of true solution. But, at the side of ions and of molecules, the U-colloid appears very soon and prepares the precipitation. The precolloidal opalescence is a proof that between molecule and colloid there exists an intermediate state—that of molecular aggregate. When the colloids pass into solution, they follow the same way, but quite in the reverse direction: colloid, molecular aggregate, molecule, ion. The stability of ions and of molecules in the oversaturated solution is greater than that of colloid; consequently, the greater the quantity of colloid in an oversaturated solution, the more rapid is the precipitation; the formation of colloid consecutive to the state of balance maintains constant the process of precipitation. The colloid is then decisive for the degree of constancy of the U-oversaturation.

*Peculiarities of form of the precipitates from an oversaturated solution.* On the acid and alkaline sides, outside of the neutral zone  
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favorable to the colloid formation, a pure crystalline precipitate appears; in the N-zone, we have only colloid elements in form of drops. There exists, however, on both sides of the N-zone, a transitional zone into which the crystalline precipitate presents itself as spherical or grass-like groups. It is only on this side of these transitional zones that isolated crystals are to be found. As the jelly becomes old, the drops increase in size through confluence and apposition and, at the same time, they receive a crystalline frame. In this way they are transformed into the well-known spheroliths.

*The uric acid colloid as cause of the abnormal persistence of the dissolved state of the U-oversaturations.* The true solubility is characterized by the state of dispersion of the ions (or molecules); between the limit of solubility and the cloudiness visible to the human eye, there exists for the colloids an intermediate state, in which the fluid still appears as being quite clear but in which there is not any true solution. This is the so-called state of persistence of dissolved state. The curve of this state depends on the concentration of H-OH ions; that dependence follows the curve of the conditions favorable to formation of colloids. It is always easy to prove the presence of U-colloid in the U-oversaturations of high and middle grades. In the lowest grades of oversaturation, one succeeds also in proving this presence, eventually, with the help of centrifugalization and artificial acceleration of the separation (through cooling). The peculiar persistence of dissolved states of uric acid in oversaturations into the N-zone depends therefore, on the U-colloid being particularly favored in that zone. The manner of preparation of the oversaturated solution (uric acid or urate as the fundamental body) does not play any rôle, provided that the correct concentration of H-OH ions be obtained.

*Causes favorable to the formation of U-colloid in the N-zone.* Investigations show that the N-zone is, at the same time the zone in which acid and salt exist, side by side, in the solution, and that in the precipitates, there exists a mixture of acid and salt. As the mixtures pass into the crystalline state more slowly than pure substances, the possibility of the separation of colloids (or of larger drops) is increased within the limits of this zone.

*Behavior of the U-colloid outside of the N-zone.* When the temperature becomes lower, we observe an enlargement of the zone of appearance of colloids. At 37°, C, we may already observe the coöperation of a process of separation, in the shape of drops, when the precipitate forms. If, however, the temperature of the oversaturated solution (which has been prepared with the aid of heat) is rapidly lowered down to 0°, the U-colloid, or the U-jelly, appears and is widely independent of the N-zone.

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**Protein Ion Mobility.**

*Wolfgang Pauli, Biochem. Ztschr., 127:150, Berlin, Feb., 28, 1922.*

The mobility of protein ions could only be taken into consideration after more exact conceptions of the constitution of protein ions had been gained, which permitted of definite deductions regarding the protein ion concentration of a solution. It is this concentration, however, whose product with the mobility yields the electric conductivity, which is the quantity most amenable to measurement. Sven Odin and

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Pauli investigated the potentiometric measurement of the ionic concentration  $C_H$  and  $C_{re}$ , in the case of acid proteins. Of the free Cl ions the concentration  $C_H$  is to be apportioned to hydrochloric acid and  $C_{re}$ , to  $C_H$  to the protein salt, so that  $C_{re} - C_H$  denotes the concentration of free protein ions. The total conductive capacity K is the sum of all products of the mobilities (u,v) and of the concentration C of the different ions, so that the mobility of protein ions remains as the unknown quantity.

The experiments carried out with albumin and glutin show that the average protein ion mobility rises with increasing acid absorption up to a maximum which is found graphically at 33 rheostatic Ohms at 18° C. and may be assumed to be 38 at 25° C. In accordance with the latest electrochemical data the molecular weights of globulin and casein are 12,000 and 3000 respectively. On the assumption that no constitutional difference exists between positive and negative ions which would alter the molecular dimension, the valency of such positive protein ions may be determined from the combined acid, the values obtained for negative ions being confirmed in this way. It is possible, therefore, to compare large organic ions having the same constitution and number of atoms, and differing only in the symbols of their electric charge, as regards their mobility and other physicochemical properties.

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**A Chemical Study of the Proteins of the Adzuki Bean, Phaseolus Angularis.**

*D. Breese Jones, A. J. Finks and C. E. F. Gersdorff, J. Biol. Chem., 51:103, March, 1922.*

The adzuki bean meal used for the preparation of the proteins contained 21.13% of protein. Preliminary experiments showed that the maximum amount of protein was extracted by thoroughly mixing the meal with aqueous 5% sodium chlorid solution in the proportion of 4 c.c. of solvent to each gram of meal, and allowing the mixture to stand for forty hours in cold storage at 1°-3° C. It was found that if the extraction was allowed to take place at room temperature, a smaller yield of the alpha globulin was obtained. This globulin denatures readily, changing into an insoluble form, a tendency which is less marked at a low temperature. In this way 79% of the total protein in the meal was dissolved, or 16.7%, based on the amount of meal used. By applying to the adzuki bean the same methods used in the authors' laboratory to separate the globulins of the mung, navy, and lima beans, it was possible to isolate two globulins closely resembling the globulins obtained from those beans. Both globulins gave positive tests for tryptophan, and 2.13% tyrosin was isolated from the beta compound. The alpha globulin was precipitated by addition of ammonium sulphate in sufficient amount to make the original extract 0.3 saturated. A small fraction, consisting of a mixture of the 2 globulins, was separated from the filtrate by increasing the concentration of ammonium sulphate up to 0.65 of saturation. This fraction was discarded, and the beta globulin precipitated by making the solution completely saturated. A small amount of an albumin was found in distilled water extracts of the bean, after the globulins had been re-

moved. The 2 globulins were found to differ markedly in their sulphur and nitrogen content and in their nitrogen distribution as determined by the method of Van Slyke.

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**The Nitrogen Distribution of Proteins Extracted by 0.2 Per Cent Sodium Hydroxid Solution from Cottonseed Meal, the Soy Bean, and the Cocoanut.**

*W. G. Friedmann, J. Biol. Chem. 51:17, March, 1922.*

The object of this investigation was the determination of the proteins of cottonseed meal, the soy bean, and the cocoanut precipitable by slightly acidifying the alkaline extract. The proteins were extracted by shaking the fat-free meal (60-mesh sieve) with a small amount of 0.2% sodium hydroxid solution and several drops of alcohol for five minutes, centrifuging the extract, and shaking the residual meal for several hours with a small amount of dilute sodium hydroxid solution. The proteins were precipitated by acidifying the alkaline extract to 0.1% acidity with dilute acetic acid. Of the precipitated proteins 4 gm. were taken for the determination of the nitrogen distribution.

When alcohol was added to the concentrated unprecipitated nitrogen fraction no precipitate formed, with the exception of a small amount from the soy bean which was added to the precipitable proteins of the soy bean. When the soluble nitrogen fraction was dialyzed no precipitate formed. Before hydrolysis with hydrochloric acid, the amino-nitrogen of the soluble nitrogen of cottonseed meal was 6.25 c.c. at 21° C. and 741 mm., and after hydrolysis, 17.20 c.c. at the same temperature and pressure in the same volume of solution. A solution containing 0.26 gm. of soluble-nitrogen obtained from the cocoanut gave 4.9 c.c. of amino-nitrogen before hydrolysis and 50 c.c. of amino-nitrogen after hydrolysis at the same temperature and pressure. These results show that proteins are present in the soluble nitrogen fraction.

The 5% barium hydroxid solution to which 1% alcohol was added by volume extracted 74.3% of the total nitrogen of cottonseed meal. The protein precipitated from the 0.2% sodium extract and the precipitable protein from the 5% barium hydroxid extract had the same nitrogen distribution as that of the globulin. The nitrogen distribution of the precipitable proteins in the 0.2% sodium hydroxid extract of the soy bean showed a somewhat similar distribution to that of the globulin (glycinin). No difference in the nitrogen distribution of precipitated protein containing 50, 65, and 78% of the total nitrogen of the cocoanut was observed. The protein of the cocoanut precipitated from the 0.2% sodium hydroxid extract by acidifying with dilute acetic acid differed markedly from cocoanut globulin in the arginin nitrogen value.

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**The Green Respiratory Pigment and Its Significance in the Oxidation of Albuminoids in the Germinating Seeds of *Helianthus Annuus*.**

*Alexander Oparin, Biochem. Ztschr., 124:90, Berlin, Nov. 21, 1921.*

The seed of the sunflower contains a body which in its properties  
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is closely related to tannic acid. It is derived in crystals, called chlorogenic acid and expressed in the formula  $C_{32}H_{32}O_{10}$ . The power of an alkaline solution of the chlorogenic acid to color green in the presence of oxygen suggests the possibility of its being a respiratory pigment. In order to obtain definite conclusions on this subject, the power of a chlorogenic acid solution to absorb oxygen was tested quantitatively. In one method the chlorogenic acid solution was put into the eudiometer and the absorbed oxygen was measured: every molecule of chlorogenic acid absorbed 2 atoms of oxygen. With the other method the completely oxidized chlorogenic acid was converted into potassium salt and analyzed.

The oxygen does not combine directly with the molecule of the chlorogenic acid, but takes 4 atoms of hydrogen away from the latter. This oxidizing process can be strengthened 20-fold by the addition of a small amount of phenolase from the seed of the sunflower. An attempt was made to determine to what extent the green pigment can promote the oxidation of food substances in the germinating seed by oxidation tests with amino-acids, polypeptides, peptons and albuminous bodies, the following natural amino-acids being used: glycocoll, alanin, leucin, asparaginic acid, glutamic acid, tryptophan and prolin. In every case the appearance of ammonia, carbonic acid and aldehyds of the lower fatty series was determined. In the presence of carbonic and phosphoric acids the reaction progresses much more rapidly. For the quantitative tests, 0.15 c.c. amino-acid and 0.1 c.c. chlorogenic acid were mixed in watery solution which was slightly alkalinized by the addition of soda and left standing in a warm place for four days; the resulting ammonia was distilled off and absorbed in N/10  $H_2SO_4$ ; the residue contained aminonitrogen; 10-20% of the used amino-acids became oxidized.

Oxidation tests with amino-acids in peptone showed that ammonia and other decomposition products resulted. Undoubtedly all the albuminous split products and the albumin itself are oxidized in the presence of chlorogenic acid with the liberation of ammonia. In order to learn more about the process of retrogressive metamorphosis of albumin in the germinating seed in the simultaneous action of proteolytic ferment and an oxidizing agent like chlorogenic acid, experiments were conducted to determine: (1) the simultaneous effect of proteolytic ferment prepared from the seed of the sunflower, and the chlorogenic acid effect upon albumin; (2) an autolysis of the germinating seed; and (3) the effects on the living seed. In the technic adopted the albumin was coagulated by cooking in a solution acidulated with acetic acid, the peptone was precipitated by colloidal iron hydroxid and the filtrate was analyzed by the van Slyke method; in another portion of the filtrate, the hexone bases were precipitated by phosphotungstic acid and the ammonia of the filtrate was determined by Sachsse's method; the residual fluid after the removal of ammonia was hydrolyzed in concentrated hydrochloric acid and the ammonia and aminonitrogen were determined in the hydrolysate. The resulting figures show that in the simultaneous presence of chlorogenic acid and oxygen, more free ammonia, and ammonia and aminonitrogen result from hydrolysis than in the absence of one or the other components. During the simultaneous action of proteolytic ferment and the oxidizing agent of the germinating seed, the contained albuminous bodies decompose with separation of the amino-groups as ammonia.

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The Preparation of Inulin, with Special Reference to Artichoke Tubers as a Source.

*J. J. Willaman, J. Biol. Chem., 51:275, March, 1922.*

On the basis of these experiences, the author recommends the following procedure for the preparation of inulin from artichoke tubers: Grind the washed tubers as fine as possible, and put into boiling water containing calcium carbonate. For each kilo of tubers use 1300 c.c. water and 30 gm.  $\text{CaCO}_3$ . Boil fifteen to twenty minutes, extract the juice with a press, reboil with 1000 c.c. water and 10 gm.  $\text{CaCO}_3$ , extract, and combine the extracts. Clarify with lead acetate, avoiding a large excess. Centrifuge, or filter, remove the lead with ammonium oxalate, and centrifuge again. The clear liquor may here be treated with decolorizing carbon, although this is usually not necessary. It is then evaporated under vacuum to a content of 40 to 60% solids. This syrup is allowed to cool slowly, then it is kept at 0-5° C. for several hours, thoroughly stirred with an equal volume of ice water, and centrifuged. The crystals are redissolved in about 3 volumes of water, filtered hot, concentrated to about twice the volume of the original crystals, and allowed to crystallize in the cold as before. They are again stirred with ice-water, filtered on paper or on silk bolting cloth by suction, keeping everything as cold as possible. The crystals are washed with cold water, then with 20, 50, 80, and 95% alcohol and ether, and dried in an oven at 100° C. The specific rotation of the preparation should not be less than —33°. A third crystallization may be performed, although it is useless to attempt to obtain a higher rotation than —38° or —39°.

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Do the Amino-Acids Occur in Cow's Milk?

*Yoshizumi Hijikata, J. Biol. Chem., 51:165, March, 1922.*

Van Slyke's method is by no means so specific as to enable an investigator to locate with certainty any traces of aminonitrogen in milk. The presence of amino-acids in milk may not be considered proved until they have been isolated and characterized. By means of a special method the author has demonstrated the following amino-acids in cow's milk: lysin, arginin, and histidin. Mono-amino-acids are probably also present. In addition to the amino-acids enumerated, guanin, adenin and cholin were found.

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The Synthesis of 2-Hexosamino-Acids and 2-Hexosamins.

*P. A. Levene, Biochem. Ztschr., 124:37, Berlin, Nov. 21, 1921.*

The problem of the identification of any one of the still unknown 2-aminohexoses consists of two parts: (1) the explanation of the structural formula in respect to carbon atoms 3, 4 and 5, and (2) that of the structural formula in respect to carbon atom 2. From the equilibrium of the epimers, which form from the condensation of the pentoses on the one hand and from the aminopentosides on the other, with hydrocyanic acid, and also from the study of the optical deviation of the

hexosamino-acids, and finally from the observation of Walden's reversal, the structural formula of the 2-aminohexonic acids may be reached through the following juxtaposition:

chitosamino-acid	2-aminomannonic acid
epichitosamino-acid	2-aminogluconic acid
chondrosamino-acid	2-aminotalonic acid
epichondrosamino-acid	2-aminogalactonic acid
dextro-d-xylohexosamino-acid	2-aminogulonic acid
levo-d-xylohexosamino-acid	2-amino-idonic acid
dextro-d-ribohexosamino-acid	2-amino-allonic acid
levo-d-ribohexosamino-acid	2-amino-altronic acid

None of the 3 different formulas which have been proposed for the structure of amino-derivatives (namely, those of Lobry de Bruyn, of Wohl, and of Irvine, Thomson and Garret) can be corroborated experimentally.

The synthesis of the 2-aminohexonic acids from the aminopentosids was accomplished by their condensation with hydrocyanic acid; the separation of the 2 epimers formed in the synthesis was accomplished by fractional crystallization. For the purpose of final purification, the acids, whenever possible, were transformed into crystallizable derivatives. The behavior with benzaldehyd was also determined, as often 1 epimere unites with benzaldehyd, whereas the other does not combine with it under similar conditions, but gives an unsubstituted lacton. The lyxo-d-hexosamino-acids form no crystallizing lacton ester or benzylidene derivatives; but the levo-d-lyxohexosamino-acid is transformed by the action into a crystalline hydrochlorate of the sugar, whereas its epimere does not form such a product. In this way it was possible to obtain the material desired for testing the purity of each epimere of the 4 pairs of d-hexosamino-acids.

If nitrous acid is allowed to act upon a given hexosamin, 2 epimeric acids are obtained. If chitosamin is first deaminized to chitose and then oxidized to acid, the end-product is chitonic acid; but if chitosamin is first oxidized to chitosamino-acid and then deaminized, chitaric acid is formed. As these 2 end-products are both 2, 5-anhydrous hexonic acids, a knowledge of their structural formulas would throw light on the position of carbon atom 2 in the original hexosamino-acid. The structural formula of the hexose series was worked out by Fischer on the basis of their mutual relationships to the tetra-oxy-adipinic acids; in the same way, the structural formula of the 2, 5-anhydrous hexonic acids may be derived from that of the 2, 5-anhydrous adipinic acids. By a series of deaminizations and oxidations, it became evident that it was possible to pass from one hexosamin to the 2 resulting epimeric 2, 5-anhydrous hexonic acids. The transformation was accomplished by heating for four hours with an aqueous solution of pyridin at 100-105° C. A mixture of chitosamino-acid and epichitosamino-acid was obtained. The latter was purified by transforming it into its lacton. The melting point of epichitosamino-acid was 198° C. (uncorrected). It was found possible to prepare the hexosamino-acids from the l-aminopentosids; the 2 epimers, chondrosamino-acid and epichondrosamino-acid, were separated from the resulting mixture by fractional crystallization, the deflection of polarized light being used as the criterion of identity and purity. To produce the lactons of

the hexosamino-acids, the latter were several times recrystallized, dissolved in alcohol; dry hydrochloric acid gas was then added and the resulting glucosamin hydrochlorate was then reduced to sugar with sodium amalgam; the end of the reaction was determined with Fehling's solution; it was possible to produce the glucosamin hydrochlorate directly from the reduction products, in pure form. From this glucosamin hydro-chlorate directly from the reduction products, in pure form. From this glucosamin hydrochlorate a pentabenzoyl derivative was produced. In an analogous way, lyxosamino-acid was produced from chondrosamin. In the same way, epichitosamin and dextroxylohexosamin were made from the corresponding acids and the sugar derived therefrom by reduction was determined by the osazones.

Chitonic acid was oxidized to 2, 5-anhydrous oxalic acid from 2, 5-anhydrous pentoxyacpronic acids, so that the structural formula of anhydrous mannonic acid may be applied to chitonic acid and the structure of anhydrous gluconic acid to chitaric acid. Moreover, 2, 5-anhydrous talonic acid and 2, 5-anhydrous galactonic acid were produced from chondrosamino-acid and epichondrosamino-acid respectively in the form of their brucin salts. The 2, 5-anhydrous oxalic acid was produced from 2, 5-anhydrous tetra-oxy-adipinic acid by deaminization of chitosamino acids with silver nitrate and subsequent oxidation of the potassium salt, by the addition of potassium hydroxid. The potassium salt was transformed into a lead salt with lead acetate, and the free acid resulted. The 2, 5-anhydrous oxalic acid was formed by the oxidation of dextro-d-xylohexosamino-acid lacton and of the levo-d-xylohexosamino-acid. The levo-d-xylohexosamino-acid was deaminized, oxidized and the potassium obtained. This acid has the structural formula of anhydrous gluconic acid and its epimers have the structural formula of anhydrous mannonic acid and of anhydrous idonic acid, respectively. The 2, 5-anhydrous ido-oxalic acid was obtained by oxidation of the dextro-d-xylohexosamino-acid. The 2, 5-anhydrous mucic acid was obtained from the synthetic levo-d-ribohexosamino-acid and the 2, 5-anhydrous d-talonomic acid from the synthetic dextro-d-lyxohexosamino-acid and from dextro-d-ribohexosamino-acid. The epichitoses were obtained from epichitosaminohydrochlorate by treatment with mercuric oxid and precipitation with sulphureted hydrogen in the filtrate.

The chitosaminoheptonic acid was obtained from the 3-aminoheptonic acids by dissolving chitosaminohydrochlorate in water and digesting for an hour at 30° C. with hydrocyanic acid and ammonia; barium hydroxid was then added to this solution and worked up in the usual way. The levo-d-chondrosaminoheptonic acid with a melting point of 139° C., and the dextro-d-chondrosaminoheptonic acid with a melting point of 65° C., were obtained in an analogous way, from the chondrosaminoheptonic acids.

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**The Determination of the Tyrosin Content of Proteins.**

*Otto Fürth and Walter Fleischmann, Biochem. Ztschr., 127:137, Berlin, Feb. 28, 1922.*

For the determination of the tyrosin content in proteins the following methods are available. Folin and Denis's colorimetric method depends on the color reaction obtained with tyrosin by a reagent com-

posed of sodium tungstate, phosphoric acid and phosphomolybdic acid. Gravimetrically, tyrosin was estimated by weighing tyrosin separated by hydrolysis. Miller and Plimmer and Eaves made use of the capacity of tyrosin for constant bromin addition for estimating this amino-acid in proteins. Weiss has described a new method based on Millon's colorimetric process. Finally, the capacity of tyrosin to yield colored compounds (diazonium compounds) in the diazotizing experiment, after removal of histidin from a mixture of hydrolyzed albumins by precipitation with phosphotungstic acid, was utilized for a colorimetric method.

As these different methods gave different values comparative estimations were carried out with all. For this purpose experiments were undertaken with pure tyrosin solutions, tyrosin estimated in casein, and blood albumin estimated in keratin, fibrin, conglutin and ovalbumin. It was found that the values obtained by the gravimetric methods of estimating tyrosin in proteins were clearly too low in many cases because tyrosin does not readily crystallize completely from the hydrolysates. The colorimetric methods based on Millon's reaction and on the diazo-reaction permit of only approximate estimations but are very serviceable for these purposes. The values obtained with Folin and Denis's colorimetric method are too high. Most confidence can be reposed in the bromin addition method with the reservation that some proteins seem to possess in their hydrolysates a bromin addition capacity the high degree of which is not so far sufficiently explained by tyrosin, nor by histidin or tryptophan. At any rate the bromin addition capacity of the albuminous hydrolysates, freed from all substances precipitable by phosphotungstic acid, appears to be a convenient and distinct means of detecting and characterizing proteins. Where the bromin, diazo and gravimetric methods, and Folin and Denis's method, yield concurrent values, as in the case of silk fibroin, the tyrosin value is to be regarded as definite. As tryptophan, tyrosin and cystin may be estimated approximately in proteins the values so obtained serve to determine approximately the molecular relation of tryptophan to tyrosin to cystin.

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**Colorimetric Tests for Tyrosin and the Protein Phenol Index.**

*P. Thomas, Ann. de l'Inst. Pasteur, 36:253, Paris, March, 1922.*

A separate colorimetric test for each amino-acid is highly desirable, but difficult to devise. At present, there are colorimetric tests only for tyrosin, tryptophan and histidin. The test of Folin and Denis and the Hoffmann-Millon reaction are critically examined, the results being tabulated. Folin and Denis's method is insufficient. A method based on the Hoffmann-Millon reaction is insufficient for the determination of tyrosin, but permits determination of a phenol index, characteristic of every protein. This index represents the total phenol compounds produced by hydrolysis of the given protein in comparison with tyrosin, to which is given a value of 100. The given protein is carefully dried, finely powdered and heated at 100°-105° C. until the weight is constant. Of this 2 gm. are placed in a long-necked flask, with 3.5 c.c. pure concentrated sulphuric acid and 21.5 c.c. water. Boiling is maintained twelve hours, a Hopkins cooling device surrounding the neck (Sec. 1—Page 889)

of the flask. After cooling, the liquid is filtered into a wide-necked graduated flask holding 100 c.c. The precipitate is washed with as little water as possible.  $H_2SO_4$  is precipitated as completely as possible with hot concentrated solution of BaOH, free from carbonate; theoretically 21 gm. are required. When the reaction becomes neutral, a few more drops of BaOH are added and the liquid again neutralized with dilute  $HNO_3$ . The liquid is then cooled and agitated; 2 c.c.  $HNO_3$  and water to make 100 c.c. are added. After mixing, the liquid is allowed to stand, then filtered through a Joulie funnel, or by means of a pump or centrifuge. Of the filtrate 50 c.c. is placed in a graduated flask and precipitated with a 20% solution of pure mercuric nitrate to remove tryptophan. Excess must be avoided. The liquid is cleared, if necessary (by a pinch of animal charcoal), made up to 55 c.c., mixed and rapidly filtered. No turbidity should then be produced by mercuric or barium nitrate. Of this liquid 10 c.c. is mixed with 2 c.c. Millon's reagent and examined with Duboscq's colorimeter, 4 readings being taken. The  $HNO_3$  employed should be freed from  $HNO_2$ , by agitating with finely powdered urea, distilling in a vacuum and protection from the light. The mercuric nitrate should also be heated with urea and filtered. Comparison should be made with a solution of pure tyrosin in 2% nitric acid, freshly prepared and mixed with Millon's reagent as in the solution examined (2 c.c. per 10 c.c.). A standard color may be made from xylidin Ponceau, naphthol S yellow and indigo-carmin. For the readings, a thickness of 10 mm. is best. The tyrosin content of proteins is at present obtained by gravimetric methods. The studies of Abderhalden and Fuchs show that the figures so obtained should be revised, especially for proteins rich in lysin.

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**Melanic Acids and Their Action in the Animal Body.**

*O. Adler and W. Wicchowski, Arch. f. exper. Path. u. Pharmakol., 92: 22, Leipzig, Feb. 28, 1922.*

Melanic acids are prepared by the oxidation of the aromatic cleavage products of albumin, tyrosin and tryptophan, with hydrogen peroxid in the presence of iron chlorid dissolved in lye, precipitated repeatedly with hydrochloric acid and finally examined in a 1% sodium hydroxid solution. This preparation is called tyrosin-melanin-natrium. Corresponding melanic acids are prepared from lignite and from powdered tropaeolum by solution in NaOH. All had the following chemical characteristics: (1) acid character; (2) colloid nature; (3) free acids insoluble in  $H_2O$ , alcohol or ether; alkaline salts soluble in  $H_2O$ ; (4) many reduce ammoniacal silver solution; (5) the color of the acids and salts is brown or black; (6) they inhibit blood coagulation.

The coagulation of blood is entirely inhibited by the addition of 1 mg. tyrosin-melanin-natrium or naphtalin-melanin-natrium to 1 c.c. blood in the test-tube. Neither the addition of calcium salts nor of tissue extracts can inhibit this characteristic of melanin. In rabbits when a 1% tyrosin-melanin-natrium solution is injected, about 1 mg. to 1 c.c. of blood, the blood does not coagulate for the next twelve to twenty-four hours. The solution has no effect on blood pressure, respiration or pulse. Certain doses of melanic acids kill the animals.

This effect is probably dependent on the disappearance of thrombocytes from the blood after the injection of melanic acids. The thrombocytes decrease after a short time to  $\frac{1}{50}$  normal. On necropsy of these animals, hemorrhages are found beneath the skin and different mucous membranes, so that the picture is similar to that in hemorrhagic dia-thesis. There is probably also injury of the blood vessels.

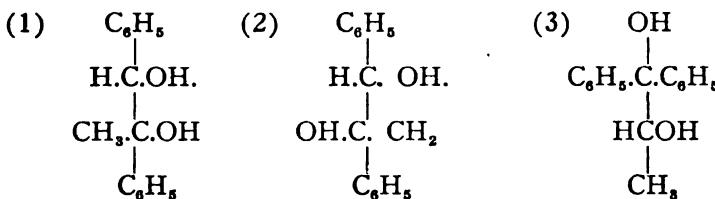
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**Carboligase. III. The Structure of Biosynthetically Linked Multiple Carbon Chains.**

*Carl Neuberg and Heinz Ohle, Biochem. Ztschr., 127:327, Berlin, Feb. 28, 1922.*

A yeast ferment produces a nuclear synthetic combination of different carbon chains. If, for instance, a fermenting solution of sugar or pyroracemic acid receives an addition of benzaldehyd, a ketone alcohol is formed whose structural formula may be either (1)  $C_6H_5.CO.CH_2OH$ , or (2)  $C_6H_5.CHOH.CO.CH_3$ . Formally this body consists of one molecule benzaldehyd and acetaldehyd. But, under the influence of the ferment carboligase not the preformed benzaldehyd and acetaldehyd enter into combination, but acetaldehyd in a preliminary stage, ready to react and produced intermediately during fermentation, must somehow form the carbon chain. In the case of carboligase a combination is effected between two bodies which show no affinity to each other, and which, so far as is known, do not combine voluntarily in the manner stated. Furthermore, the carboligastic products cannot be again split by fermentation, but are very stable substances not tending to spontaneous disintegration. In order to elucidate the constitution phenyl-magnesium bromid was allowed to act on  $C_6H_5.CO.CH_2OH$  which may lead to the formation of the following combinations.



Which of the first two formulas occurs is a matter of indifference. But from both formulas the common derivative, the optically inactive ketone  $C_6H_5.CO.CH(CH_3)(C_6H_5)$  was prepared.  $C_6H_5.CO.CH_2OH$  yields the optically active third combination. On boiling with dilute sulphuric acid the first two combinations are converted into methyl-phenyl-acetophenon (methyl-desoxybenzoin)  $C_6H_5.CO.CH(C_6H_5)_2(CH_3)$ , whose semicarbazone melts at 194° C. The third combination, on corresponding treatment with sulphuric acid, yields asymmetric diphenylacetone  $(C_6H_5)_2CH.CO.CH_3$ , whose semicarbazone volatilizes at 170° C.

It is probably permissible to assume that the ketol produced by the action of carboligase has the constitution of the pyroracemic alcohol  $C_6H_5.CHOH.CO.CH_3$ , phenylized by the liberated carbon atom.  
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The biochemic synthesis probably takes place with the help of one molecule water. The benzyl-methyl-ketone was prepared in accordance with Metzner's directions by the reaction of phenyl-acetyl-chlorid with sodium malonic ester and subsequent cleavage of the condensation product by boiling with 20% HCl. The ketone alcohol distilled over at 143°-145° C at a pressure of 31 mm. To determine the constitution the influence of phenyl-magnesium bromid on the ketone alcohol prepared synthetically from bromin propiophenon was selected. The conditions are however somewhat complicated. Under the influence of carboligase on benzaldehyd and pyroracemic acid there is formed levorotatory phenyl-pyroracemic alcohol  $C_6H_5\text{CHOH.CO.CH}_3$ . On the addition of phenyl-magnesium bromid this yields active dextrorotatory  $\alpha$ -methyl- $\alpha$ - $\beta$ -diphenyl-ethylenglycol  $C_6H_5\text{CHOH.C(OH)(CH}_3)_2(C_6H_5)$ , which, on treatment with dilute sulphuric acid, was converted into methyl-phenyl-acetophenon  $C_6H_5\text{CO.CH(C}_6H_5)$  and identified as semicarbazone. The product of the biosynthesis is therefore 1-phenyl-acetyl-carbinol.

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**The Carbohydrate Content of the Seed of Asparagus Officinalis L.**

*W. E. Cake and H. H. Bartlett, J. Biol. Chem., 51:93, March, 1922.*

Seeds of *Asparagus officinalis L.* were separated from foreign matter and ground in large mill until fine enough to pass through a 40 mesh sieve. The sample was thoroughly mixed and kept in a sealed jar until needed for use. A preliminary examination of the sample so prepared was made according to the methods of the Association of Official Agricultural Chemists, except that for the determination of nitrogen, used in computing the "crude protein", the iodometric method of Willard and Cake was used. Then qualitative experiments were first conducted in order to determine what sugars were produced by acid and enzyme hydrolyses of the asparagus seeds, followed by quantitative examination of the carbohydrates in the ether-extracted samples. From the quantitative examination of asparagus seed it was learned that the reserve carbohydrate is in the form of hemicelluloses, which give, on hydrolysis, mannose, glucose, fructose, and galactose. The galactose is in such small quantity that it probably forms part of a different hemicellulose from that which constitutes the bulk of the reserve carbohydrate. The mannose is in a ratio of 1:1 to the total remaining hexoses. The absence in appreciable quantity of carbohydrates having the properties of cellulose, starch, and inulin makes it likely that the hemicelluloses are either glucomannans occurring with fructomannans or else glucofructomannans.

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**A Change in Glycogen from Exposure to Light.**

*Gustave Bayer, Biochem. Ztschr., 124:97, Berlin, Nov. 21, 1921.*

It was noticed that a preparation of glycogen preserved in a clear glass bottle was insoluble in water, whereas one kept for the same (Sec. 1—Page 892)

length of time in a dark brown bottle was completely soluble. An attempt was made to determine the effect of light on 2 other specimens, one of which was kept in the light and the other in the dark. The same changes as before were found regarding solubility. The process of becoming insoluble may be due to polymerization, but it was noticed that here there was no decrease in the number of molecules as is usual under the effect of light energy. It must be assumed as more likely that this variation in the glycogen is the result of a purely physical change of condition in the sense of an ageing, perhaps the alteration of soluble hydrophilous surface complexes into bodies more waterless and nonswelling and which therefore, are not soluble.

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**Note on the Preparation of Mannose.**

*E. P. Clark, J. Biol. Chem., 51:1, March, 1922.*

Clark has prepared mannose by a process which, when applied to ivory nut shavings that have first been treated with sodium hydroxid, gives a yield that is considerably higher than either of the previous workers in this field (Hudson and Sawyer) has reported. The method is as follows: Sifted ivory nut shavings are added to 10 times their weight of boiling 1% sodium hydroxid solution. The mixture is at once removed from the source of heat and stirred occasionally during one-half hour. The shavings are then washed thoroughly with running water until neutral and clear, and dried. Then 500 gm. of the material thus prepared are thoroughly mixed with 500 gm. of 75% sulphuric acid and allowed to stand until the next day. This mass is dissolved in water, making a volume of 5.5 liters, and boiled under a reflux for two and one half hours. While the liquid is still boiling, it is neutralized with a thin paste of precipitated barium carbonate. The solution is at once filtered through a thin layer of active carbon placed on moistened filter paper in a Buchner funnel. The filtrate generally contains a little barium, probably in combination with organic acids. This is removed by adding a few centimeters of dilute sulphuric acid until no further precipitate is formed. The barium sulphate is filtered off and the solution evaporated under reduced pressure to 87-88% total solids. An equal volume of glacial acetic acid is added and thoroughly mixed by warming and shaking. The syrup is seeded, placed in an ice box over night for crystallization to start, and it is then frozen with an ice-salt mixture. The frozen mass is placed in a refrigerator at or near 0° C. where it will thaw out slowly. After about a day the greater portion of the sugar will often have crystallized, but generally a week is required for complete crystallization. The yield is uniformly 42 to 45% of the treated meal used.

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**A New Method of Pepsin Estimation.**

*Karl Glässner, Biochem. Ztschr., 127:314, Berlin, Feb. 28, 1922.*

The estimation of pepsin is affected either by measuring the decrease of a solid albuminous substance under the influence of the ferment, or by the precipitability of a dissolved albuminous substance as a measure of the amount of pepsin. A method is described which  
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depends on the fact that globin is precipitated from hydrochloric acid solution by ammonia, and is not dissolved by excess of ammonia, particularly if a few drops of ammonium chlorid solution be added. The chief difficulty was in the preparation of the globin solution for which Strauss and Grützner's method was used. The experiment is carried out as follows. Into 3 separate test-tubes are placed (1) 2 c. c. filtered gastric juice; (2) 1 c. c. N/10 HCl; (3) 1 c. c. undiluted gastric juice. These are mixed and 1 c. c. of the mixture transferred to another tube, and a series of 10 dilutions is made to obtain a progression of 1, 1/2, 1/4, 1/8, 1/16, 1/32, 1/64, 1/128, 1/256, and 1/512. The tubes are placed in a water-bath for fifteen minutes at 40° C. To each tube is added 1 c. c. of 1% globin solution. The tubes are then removed and after addition of 3-5 drops 10% ammonium chlorid solution they each receive 1-2 c. c. of 1% ammonia. A precipitate is produced in those tubes which still contain undigested globin. If the dilution limit of normal gastric juice be taken as 200, and if this figure be designated by 100%, the relative percentage of a pepsin solution as compared to normal gastric juice can be determined. The entire estimation can be completed in half an hour.

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**The Action of Pepsin and Trypsin on Diastase.**

*W. Biedermann, Biochem. Ztschr., 127:38, Berlin, Feb. 28, 1922.*

The activated ferment is not limited to a definite hydrogen-ion concentration but it is also capable of displaying its action with neutral, acid and alkaline reactions, provided the ferment is present in sufficient amount. As few and contradictory observations on the action of pepsin and trypsin on diastase are available, the behavior of amylases toward proteolytic ferments was investigated. Inasmuch as a given amount of acid or alkali is the less injurious the greater the amount of ferment, the experimental method seems clearly indicated. Diastase solutions of the greatest possible concentration had to be brought up to a degree of acidity or alkalinity at which energetic proteolysis would be possible without influencing materially the diastatic power. It was shown that the alteration of the ferment assumed larger proportions only when free acid was detectable. The occurrence of free acids when hydrochloric acid is employed may be followed very easily by means of Günzburg's reagent. The action of pepsin on salivary diastase is shown by the fact that the digested sample enables strong diminution of the diastatic power to be recognized at a time at which the similarly acidified pepsin-free solution still retains its original activity. In contradistinction to this ferment, which is so easily attacked by pepsin, the same salivary diastase was wholly resistant to trypsin digestion. The diastatic action does not diminish even after many hours and the solutions continue to yield all characteristic precipitation reactions of salivary albumoses. Besides this noteworthy difference in the behavior of the diastatic salivary ferment with pepsin and trypsin, it was found that salivary diastase is capable of combining acid or alkali without affecting the diastatic power, while this occurs immediately as soon as free H ions or OH ions are present. This behavior enables the protein nature of diastase to be inferred, from which it appears also that in case similar relations exist between acid toleration and amounts

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of ferment as in the case of diastase, the same composition of another ferment may be assumed.

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**Importance of the Medium in the Study of Catalase. I.**

*Ubaldo Sammartino, Biochem. Ztschr., 126:179, Berlin, Feb. 15, 1922.*

According to Low's researches, animal and plant tissues contain a specific enzyme capable of decomposing hydrogen peroxid. The amounts of the catalases were brought into relationship with the intensity of the oxidation processes in the animal organism and it was found that the activity of catalase is usually greater in mature than in embryonic tissues and that the amount of catalase is less in fish tissue than in that of warm-blooded animals. Sperm contains more catalase than ovarian substance. Active tissue contains a larger amount of catalase. According to Senter, blood catalase is confined in the red blood-corpuscles. The results of the experiments go to show, as a whole, that the medium must exercise an appreciable influence on the formation of free oxygen from hydrogen peroxid and this was confirmed by experiments designed to study the influence of vitamins on catalase. The original method of catalase determination depends on the measurement of the volume of oxygen developed in a given time by a definite volume of blood. The researches were carried out with Schiff's azotometer in which the liberated oxygen and the reacting mixture were separated by a mercurial column. A 3% hydrogen peroxid solution and 20 c.c. 1.25% blood solution were employed. For studying the influence of vitamins on catalase, 5 c.c. vitamin solution extracted from beer yeast was put in an azotometer. The vitamin solution had a distinct acid reaction. From the tables and curves it is clear that the mixture with acid-reacting vitamin solution gave slight oxygen development, while in another case the alkaline reaction, much more so than the vitamins as such, had a pronounced influence on the reaction intensity. Consequently, acids and bases are capable of influencing the reaction velocity of catalases and according to Sörensen there exists a relationship between the hydrogen-ion concentration most favorable for catalase and the duration of the reaction. The increase or decrease of oxygen development in numerous pathologic cases obviously does not depend on an increase or a decrease of blood catalase but on the alteration of the medium which then modifies the quantity of oxygen developed in the course of the experiments. In accordance with this, the catalytic capacity in the tissues of hungering animals diminishes and the animals are capable of a certain immunity in the sense that after fasting twice their tissues are richer in catalase than those of animals fasting the first time. The acidity and alkalinity of blood and tissues are certainly of importance in the study of catalases.

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**The Lyotropic Series and— $\beta$ —Oxidation.**

*K. Spiro, Biochem. Ztschr., 127:299, Berlin, Feb. 28, 1922.*

In connection with Hofmeister's lyotropic series it is mentioned that in physiologic experiments attention was chiefly directed to potassium and calcium among cations and to chlorin among anions.

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Physiologic examples show that anions, by their influence on the process of solution, i. e., hydration or solvation, as such also exert an influence on the action of cations. To the blood  $\text{HCO}_3$ -ions, besides  $\text{Cl}$ -ions, are of importance. From the fact that no nutrient solution free from  $\text{HCO}_3$  is obtainable, the unreplaceability of  $\text{HCO}_3$ -ions is assumed. Of the anions on the thiocyanate side,  $\text{CNS}^1$  and  $\text{I}^1$  occur regularly in very small amounts in the animal body. Their action may be catalytic. The importance of  $\text{PO}_4$ -ion is due to its easy esterification with important cellular components (glucose, casein, nuclein) so that it disappears easily from the solution and reappears in a reversal of the process.  $\text{SO}_4$  stimulates yeast fermentation. The action of cations depends on the simultaneous presence of concurrent anions which agrees entirely with experiences gained with solubility in the quantitative sense.

Hofmeister's results relating to oxidation of fatty compounds tend in two directions: (1) the difference in the action of methyl and ethyl alcohol, and (2) the oxidation of most fatty acids in the beta position, or decomposition between alpha and beta carbon. It should be remembered that differences in intensity of solution are to be regarded as the reason for the different chemical behavior of methyl and ethyl alcohols. Methyl alcohol mixes with water more readily than ethyl alcohol and therefore penetrates the aqueous medium with greater ease and is displaced from the same less easily. Methyl alcohol clings to the cell more tenaciously and once it has penetrated it is less easily displaced with water than ethyl alcohol. In the case of the higher fatty acids the constants fluctuate; this has been demonstrated for melting points, boiling points, solubility, molecular volume, molecular heat, dissociation constants and optical rotation. It is pointed out that the chains with an even number of carbon atoms and those with an odd number behave physicochemically like two constitutionally independent or different series. Hofmeister and his pupils have shown that the oxidation of carbon chains does not take place, as was at first assumed, from carbon atom to carbon atom, but in pairs. This is the principle of paired decomposition, which is compatible with the splitting off of single pairs (acetic acid, oxalic acid), double pairs (butyric-acid, succinic acid) and multiple pairs, inasmuch as the physicochemical regularities of the series with 2 nC atoms begin only with butyric acid. And a number of physiologic facts indicate that in addition to beta oxidation, i. e., the formation of two-chain carbon atoms, four-chain carbon atoms are also formed.

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**The Physical Chemistry of Lipoids. The Migration of Methylen-Blue Through Organic Solutions.**

*S. Loewe, Biochem. Ztschr., 127:231, Berlin, Feb. 28, 1922.*

For the examination of chemicophysical peculiarities of certain brain lipoids their behavior toward methylene-blue in the three-phase experiment was employed. To an aqueous methylene-blue solution (first phase), a lipoid solution in organic solvents (carbon tetrachlorid) (second phase) and beyond this pure water (third phase) were ranged. Herein it was possible to determine the peculiar ability of phosphatid and cerebosid mixtures to effect the entrance of the dye into the phase

of the organic solvent, which does not dissolve it in the pure state, and the passing on of the dye to the third phase. The cause of the unusual solvent mediation is certainly related to the colloidal division of the lipoid. In order to amplify the conception of the physicochemical behavior of the bodies known as lipoids the three-phase experiment was extended to as many fatlike bodies as possible. The following 29 substances were investigated: ceresin, cholesterol, cholesterol acetate, cholesterol stearate, lecithin, cephalin (crude), cerebrosid (crude), spermaceti, cetin, cera alba, cera flava, stearic acid, tristearin, tripalmitin, triolein, mastic, dammar resin, euphorbium, crude wool-fat, neutral wool-fat, wool-fat acid, hydrous wool-fat, anhydrous wool-fat, wool-wax I, wool-wax II, wool-fat stearin, wool-fat oleostearin, wool-fat olein, wool-pitch. The solvents employed were chloroform, carbon tetrachlorid, benzol, toluol and ether. Into one arm of a Y-shaped tube methylene-blue gelatin was poured, and into the other arm uncolored gelatin; after cooling these were covered with the substance to be examined. Among the pure substances examined were found an alcohol (cholesterol), an acid (stearic acid), 3 triglycerids and 2 cholesterol esters. The mixtures fell into four groups: (1) the 3 crude lipoids, (2) the 3 resins, (3) ceresin, spermaceti and its purification product, as well as wax, and (4) wool-fat products. Their solubility in the organic solvents differed in the highest concentration of 3%. The experimental results are tabulated and show, as a general result, that the parallel experiments conducted with the same substance in different organic solvents agreed in very few cases. Only ceresin was found to possess constant behavior in all solvents. From this it appears that the various organic solvents are by no means of equal value. The transmission of dye through a solvent layer that does not dissolve the dyes, which was considered so remarkable in former researches, was therefore not observed frequently in the present increased number of substances examined. It may be observed most readily with several crude products of wool-fat preparation and particularly with wool-pitch and wool-wax. In the case of two solvents it may also be observed with mastic. Closely related to mastic are substances designated as resin-like. But the chemicocolloidal peculiarities cannot be fathomed, as yet, from these researches.

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**Lipoids. XVIII. Preparation of Phosphosulphatids from the Brain.**

*Oskar Gilbert, Biochem. Ztschr., 124:206, Berlin, Nov. 21, 1921.*

An alcoholic extract was made from the dry substance of 20 fresh human brains with a weight of 5800 gm. The white substance was centrifuged with 4 kg. ether to remove the cholesterol and cephalin. The ether-insoluble portion was boiled with alcohol as long as white precipitate formed. The whole amount of the white substance, the so-called protagon, was freed of the last residue of alcohol by expression and the whole dry mass was dissolved in boiling methyl alcohol and precipitated by caustic baryta solution. The methyl alcohol was filtered off and the white precipitate was washed with water; the barium salts insoluble in alcohol were dried and were to a great extent soluble in benzol. The benzol-soluble barium salt was separated from the benzol-insoluble

salts by the centrifuge. The barium salt insoluble in benzol had a melting point of 278°C. and the benzol-soluble barium salt showed browning at 198°C. and decomposed at 215°C. As the latter was not completely purified, it was treated with petroleum ether: the barium salt soluble in benzol and petroleum ether melts at 228°C. after a previous browning at 220°; it was crystalline and may be regarded as the barium salt of brain acid. By recrystallization a white crystalline body with a melting point of 194°C. was found. The orcin reaction was negative.

Sulphur, phosphorous, nitrogen and barium were found in the barium salt of brain acid in the proportion of 1:1.3:2. An elementary analysis showed the formula  $C_{93}H_{187}N_8SPBa_2O_{18}$ . The free brain acid was obtained by treatment with hydrochloric acid. The melting point was 153°. The elementary analysis showed a formula  $C_{93}H_{187}N_8SPO_{18}$ . The proportions of sulphur, phosphorus and nitrogen were 1:1.3. The barium salt of the brain acid was hydrolyzed with hydrochloric acid, the product of hydrolysis was taken up with ether, shaken several times and the watery layer separated. A lead salt was prepared from the ethereal layer after distilling off the ether with a solution of lead acetate in methyl alcohol. The analysis showed that  $(C_{25}H_{48}O_8)_2Pb$  represented the lead salt of cerebron acid.

A platinum salt was separated from the watery layer,  $C_4H_6N_2C_6PtO_7 = (NH_2CH_2CH_2OH)_2 = 2HCl - PtCl_4$ , which equals the platinum salt of the amino-ethyl alcohol, which the analysis proved. The barium salt of brain acid was also hydrolyzed with caustic baryta. The fatty acid precipitated from the ether after recrystallization had a melting point of 100°C. and the analysis gave the formula  $C_{25}H_{50}O_8$  for cerebron acid. These substances should therefore not be considered as sulphatids but as phosphosulphatids.

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**Lipoids. XIX. Lecithin from the Human Brain.**

*S. Fränkl and A. Käsz, Biochem. Ztschr., 124:216, Berlin, Nov. 21, 1921.*

Linert prepared a substance from brain, which he called sahidin, and assumed that it was not lecithin, but a triaminodiphosphatid, which in addition to cholin contained at least one other base. Experiments were conducted to see whether, after further purification, it would not prove to be lecithin. For this purpose, the sahidin was recrystallized with alcohol containing cadmium chlorid and after several precipitations of toluol solution it was fractionated out of the alcohol by recrystallization. The resultant product had a reaction of nitrogen to phosphorous in the ratio 1:1. It was a striking fact that in the analysis of the substance previous to the precipitation of the toluol solution, values were obtained which corresponded very well with those found by Linert. The percentage of the substances which contaminate the lecithin is fairly constant and it is possible that these form mixed crystals or addition products with the lecithin cadmium chlorid. A combination with platinum chlorid was prepared, which was also purified by the precipitation of toluol solution giving the proportion N:P:Pt=2.2:1.

The hydrolysis was accomplished with a recrystallized product of alcohol containing cadmium chlorid: outside of the split products of the lecithin, only ammonio-ethyl alcohol could be demonstrated with

certainty. As the ammonio-ethyl-alcohol is the base of cephalin, the sahidin of Linert was a lecithin unpurified of its own split products. The hydrolysis products were glycerinphosphoric acid, cholin acid, stearic acid and an unsaturated oleic acid. Palmitic acid, which Levene demonstrated in the lecithin of egg yolk, was not demonstrable. The addition of the split products, after the subtraction of 3 molecules water, showed the formula  $C_{44}H_{88}NPO_9$ , corresponding to the analysis of the cadmium salt. As on the entrance of stearic acid and of oleic acid into the glycerinphosphoric acid molecule, one molecule of water is split off with each, and also one molecule with the esterization of the cholin, the described lecithin from the human brain would be a stearyl-oleyl-lecithin. These particular combinations were substantiated by analyses.

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(1b—162)

**The Unsaturated Fatty Acids of Liver Lecithin.**

*P. A. Levene and H. S. Simms, J. Biol. Chem., 51:285, March, 1922.*

In the course of the present work it was found that liver lecithin yields only 2 unsaturated fatty acids, oleic and arachidonic acids, and of these oleic acid predominates. Assuming that only 2 unsaturated acids, arachidonic and oleic acids, are present in the lecithin fraction, and taking into consideration the fact that the iodin number of the mixed unsaturated acids of this lecithin is 196, it becomes easy to calculate the ratio of the 2 acids from the equation  $90x + 35y = 196$  ( $x + y$ ). It follows that the ratio is approximately 1.3 parts of oleic acid to 1 part of arachidonic acid. The lecithin referred to above was obtained from the acetone extract of the liver. From the ethereal extract there was obtained a lecithin of lower unsaturation. The iodin number of the unsaturated acids was 136. This corresponds to 4.3 parts of oleic acid to 1 part of arachidonic acid. Bearing in mind the molecular weight estimation of dihydrolecithin reported in the authors' previous communication, namely 810, one is justified in concluding that the liver contains several lecithins and that the oleyl lecithins predominate.

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(1b—163)

**Calcium Combination with Animal Tissues.**

*E. Freudenberg and P. Gyögy, Biochem, Ztschr., 124:299, Berlin, Nov. 21, 1921.*

As the complex found in the organism would of necessity lead to calcification of tissues if no inhibitory effects came into play, attempts were made to discover substances which have such an inhibitory effect. Among these are urea and ammonia salts; anions may have such an effect and there are substances which appear with tryptic or autolytic anabolism of albumin. The experiments showed: (1) That amino-acids, peptids, also imidazol, methylamin, trimethylamin, betain, guanidin, methylguanidin and creatin inhibit the calcium combination in cartilaginous tissue; glicinanhydrid and creatinin, also cholin and adrenalin were found without effect. The former substances and caffein inhibit also the combination of calcium with the serum colloids and increase the diffusible calcium fraction in the serum. (2) That acetate and nitrate

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inhibit the calcium combination by young cartilage tissue, having been previously demonstrated, it is now established that the calcium combination from serum is diminished in the brain substance by these anions in comparison with chlorid and sulphocyanid. An increased concentration in bicarbonate and phosphate leads to an analogous diminution: this effect is considered as indirect, as the solubility and dissociation of the calcium combinations, respectively, are diminished in serum. (3) As it was found in dialysis experiments with serum that acetate and nitrate convert calcium into the indiffusible form, the diminution of the calcium combination was attributed to a second (fast) phase after deionization of calcium in the first phase as a result of complex formation with the colloids dissolved in it.

These findings may serve as the groundwork for the explanation of numerous facts in physiology, pathology and pharmacology, in their respective stimulative processes.

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(1b—164)

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#### A Simple Method for Determining Calcium in Albuminous Liquids.

*P. Cristol, Bull. d. sc. pharmacol., 29:79, Paris, Feb., 1922.*

The reagents required are 20% trichloracetic acid, 30% NaOH (sp. g. 36° B.), 2% alcoholic solution phenolphthalein, pure, and 25% sulphuric acid, 3% ammonium oxalate and one-twentieth normal potassium permanganate, of which 1 c.c. is equivalent to 0.001 gm. calcium. Exact measurement is made of 10 or 12 c.c. of serum, or other albuminous liquid, and treated with an equal bulk of 20% trichloracetic acid, agitated and filtered. Of this 10 c.c. is nearly neutralized by 9 or 10 drops of NaOH solution, diluted with about 50 c.c. distilled water, and heated to boiling. Next 10 c.c. ammonium oxalate solution is added and the mixture allowed to simmer for about five minutes. After cooling it is filtered. The precipitate is washed until the washings no longer give the test for oxalates. A heat-proof jar, containing 50 c.c. distilled water and 5 c.c. pure sulphuric acid, is then placed under the funnel; 10 c.c. sulphuric acid (25%) is poured upon the filter, which is washed twice with a small jet. The filtrate is brought to 80°C. and titrated with the permanganate. The number of milligrams Ca equals 0.001 times the number of cubic centimeters of permanganate required, multiplied by 200, or the quotient obtained by dividing the number of cubic centimeters required, by 5.

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#### 1c. PHARMACOLOGY AND TOXICOLOGY

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#### The Hemolytic Test as Criterion for the Infiltration of Pharmaceutical Substances.

*Karl Peyer, Wien. klin. Wchnschr., 35:222, March 9, 1922.*

In examining Pregle's iodin solution Peyer discovered that when brought together directly with washed red blood-corpuscles in vitro the erythrocytes were blackened and after a while hemolyzed. As this solution also attacks other cells (leukocytes in pus and sputum),  
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he concluded that Pregle's iodin solution had the property of causing infiltrations when given subcutaneously. This effect is probably due to the free iodin, because boiled Pregle's solution, which does not contain free iodin, does not show any tendency to the formation of infiltrations, or to hemolysis. In order to find out whether other substances, when given subcutaneously, also have the property of causing infiltrations and hemolysis, Peyer investigated cocaine, morphin, atropin, digalen, salvarsan, oil of camphor, turpentine, quinin, ether, dispargen, mercury preparations, and sodium cacodylate, and determined whether a previous treatment of these substances with serum destroyed their hemolytic power. All the different substances investigated showed a parallelism between hemolysis and the tendency to infiltrations, with the exception of salvarsan; all the substances which caused infiltrations also caused hemolysis in vitro. The hemolytic test is therefore important in the preparation of new drugs which are to be administered subcutaneously.

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**The Pharmacy and Chemistry of the Australian Pharmaceutical Formulary.**

*R. C. Cowley, M. J. Australia, 1:259, Sydney, March 11, 1922.*

The object of the Australian Pharmaceutical Conference in publishing this work is to attain uniformity in prescribing and dispensing unofficial preparations throughout the Commonwealth and the Dominion of New Zealand. Many manufacturing druggists in the British Isles and in America have flooded the market with proprietary remedies of a kind that can easily be prepared by any competent pharmaceutical chemist. Formulas similar in composition to such proprietary preparations are included in this formulary, and can with advantage be substituted for advertised preparations. Among more important of the listed preparations are included diluted hydriodic acid, collodion acetone, mercurial cream, elixir of calisaya, elixir of cascara, milk of magnesia, compound liniment of eucalyptus, eusol, compound solution of bromochloral, compound solution of cresol (lysol), compound solution of santal, ether soap, Dakin's solution (solution of sodium hypochlorite), compound solution of thymol, pepsin and bismuth mixture, parogens, bismuth and iodoform ointment (BIPP) and stainless iodin ointment.

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**Hydrogen-Ion Concentration Studies on Distilled Water, Physiologic Sodium Chlorid, Glucose and Other Solutions Used for Intravenous Medication.**

*John R. Williams and Madeleine Swett, J.A.M.A., 78: 1024, April 8, 1922.*

The hydrogen-ion concentration of drugs and chemicals used for therapeutic or investigative purposes is of great importance. Intravenous injection is often followed by chills and prostration. The hypothesis is advanced that when fluids of a much higher or lower concentration than that of the blood are introduced into the circulation at a rate or in an amount in excess of the capacity of the blood to buffer or neutralize them, severe reactions or death may follow. Some of the fluids in common use for hydrogen-ion concentrations are beyond the

limits of safety. By the hydrogen-ion method it was determined that distilled water if not carefully prepared or when stored as a stock solution, becomes highly acid so that when used as a solvent it may produce a solution with a much higher hydrogen-ion concentration than that of the body. Glucose solutions become highly acid when boiled, autoclaved, or permitted to stand for a few hours. Physiologic sodium chlorid solutions, when prepared with stock-distilled water or impure salt, may be very acid. It is obvious that a salt solution which is physiologically normal for the body must not only be correct in salt content but also in hydrogen-ion concentration. Tap water is much preferred to distilled water. These solutions may be easily rendered safe for therapeutic purposes by the addition of buffer salts. The buffer tablets were prepared by Dr. Slagle from monopotassium and dipotassium phosphate salts, in such proportions and amounts that when one tablet weighing approximately 0.1 gm. is dissolved in 20 c.c. of freshly distilled water, it will have a pH of the desired value.

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**The Practical Application of "Buffers" in the Regulation of the Hydrogen-Ion Concentration of Intravenous Solutions.**

*Ralph R. Mellon, E. A. Slagle and S. F. Acree, J.A.M.A., 78:1026, April 8, 1922.*

The purpose of this paper is to show how reactions from the injection of intravenous solutions may be controlled by the use of buffers and the possibility that untoward reactions may thus be diminished in number, in severity, or in both. The blood under normal conditions maintains a quite constant reaction, and this by means of the same sort of buffers that, in imitation, are employed with these solutions, just as, to use a homely illustration, the springs of an automobile absorb the shocks that would be transmitted to the occupants of the car. If we regard as shocks the hydrogen-ion, which is the cause of acidity, and the hydroxyl ion, the cause of alkalinity, we may regard as buffers any substances which will absorb such ions into their molecules. The phosphates and carbonates are familiar examples of such substances because they are salts of weak acids. Recent literature has directed considerable suspicion toward the employment of sodium citrate for transfusion purposes. For buffering phenolsulphonephthalein, phosphates, carbonates and sodium chlorids are employed. The result is a physiologic standard solution of the phenolsulphonephthalein having a pH of 7.2.

No final conclusion is reached on the subject as yet, but the clinical impressions have been very favorable.

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**The Importance of Calcium in the Slight Sensitiveness of the Toad toward Cardiac Poisons.**

*Hermann Wieland, Biochem. Ztschr., 127:94, Berlin, Feb. 28, 1922.*

The toad is particularly insensitive to its own poison (bufonin) (Sec. 1—Page 902)

as well as to all cardiac poisons. This resistance was thought to depend on retarded resorption and lesser sensitiveness. The toxicity of bufonin was therefore determined by subcutaneous injection in the toad and frog. The experiments were carried out by Straub's method. The solutions for injection were prepared from a 1% stock solution by dilution with Ringer's solution. The animals weighed about 20 gm. Doses were calculated for 1 gm. body weight.

It was found that the toad's cutaneous glandular secretion is at least 30 times less poisonous to this animal in subcutaneous injection than to the grass frog. The character of the poisoning also showed material difference. While the action of bufonin on the frog's heart is similar to that of digitalis, the ventricular systoles being increased, this tonic action of the poison becomes evident in the case of toads' hearts only to a slight degree with the highest concentrations. To a less extent the toad's resistance to poison is also displayed toward digitoxin. The extirpated toad's heart is influenced by bufonin, digitoxin and strophanthin to a much smaller degree than the frog's heart and in a different manner. Systolic increase is absent and the heart is arrested in diastole. In the experiments with barium chlorid the toad showed greater sensitiveness, the frog's heart being arrested by barium chlorid 1:250, the toad's heart by 1:750. In both species the ventricle is arrested in tonic contracture and this represents the fundamental difference between barium and the substances in the digitalin group. As calcium may be regarded in a certain sense as the hormone of cardiac muscle tonus, experiments were undertaken in this direction. These showed that the calcium optimum for the toad's heart lies at 0.02% calcium chlorid, namely the same as in the frog. But, while an increase of calcium increases cardiac muscle tonus in the frog, the tonus is diminished in the toad. On the assumption that cardiac poisons act indirectly by increasing the organ's sensitiveness to the physiologic action of calcium (Lewy) the divergent reaction of the toad's heart to bufonin and glusids is rendered comprehensible. The slight noxiousness of cardiac poisons to the toad is obviously related, also, to the paradoxic calcium effect.

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**Circulatory Disturbances from Shock Poisons. II. The Behavior of the Surviving Liver.**

*Hans Mauthner and Ernst P. Pick, Biochem. Ztschr., 127:72, Berlin, Feb. 28, 1922.*

The action of the substances known as shock poisons is governed by the behavior of the liver. That appears from the fact that in carnivora the liver becomes greatly enlarged and heavily congested as a result of poisoning by peptone, histamin and anaphylaxis, which cause a sudden lowering of blood pressure. In herbivora no such enlargement of the liver occurs. Perfusion experiments were conducted with dogs, guinea-pigs, cats, apes and rabbits for the further elucidation of this question. The animal was bled from the carotid under ether anesthesia and flushed with Ringer's solution through a cannula tied in the external jugular vein until the liver was free from blood. A cannula filled with liquid was then tied in the portal vein and connected with Mariotte bottles containing different perfusion liquids,

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serums, Witte's peptone, histamin, adrenalin, amyl nitrite, sodium nitrite, barium chlorid, pilocarpin and atropin. The evacuating cannulas were introduced into the vena cava through the hepatic veins. The amount of outflow was measured by counting the drops within half or one minute. The experiments indicate that the carnivorous liver (dog, cat, ape) reacts to perfusion with shock poisons such as Witte's peptone and histamin, or to the anaphylactic reaction, by obstructing the outflow passages in the hepatic veins, while the influx from the portal veins remains unaltered. Consequently the liver becomes immensely enlarged, and the liver capillaries are extraordinarily dilated. In those animals in which shock poisons do not lower blood pressure suddenly *in vivo* (guinea-pig, rabbit), no obstruction of hepatic veins and no hepatic congestion occur. The surviving herbivorous liver is, thus, insensitive to this influence, inflow and outflow, the same as liver volume, remaining unaltered. An important difference exists, also, between the isolated carnivorous and herbivorous livers in their behavior toward other poisons, such as adrenalin and barium chlorid. In this case the carnivorous liver becomes smaller, owing to contraction of the entire vascular region, by which inflow and outflow are equally arrested, while the herbivorous liver shows no material change in size, nor disturbance of inflow or outflow. The capacity of the liver to react to medicaments by vascular spasm seems to decrease in the order dog, cat, ape, rabbit, guinea-pig. The obstructive mechanism in the hepatic veins is of material importance to the occurrence of shock. This was confirmed anatomically by Arey and Simonds, who found the canine hepatic veins to be supplied with strong smooth musculature while this musculature was absent in the rabbit.

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(1c—172)

**The Determination of Alcohol in Solutions.**

*A. Lévéque, Bull. d. sc. pharmacol., 29:81, Paris, Feb., 1922.*

A method based on the critical temperature of a solution, as recently described by Lévéque, is applied to tinctures containing alcohol at 30°, 60°, 70° and 80°. The calculations are given in full. The 30° tincture is laudanum. For every tincture, there is a degree of alcoholic concentration below which the tincture is not acceptable. Tinctures prepared with 60° alcohol should contain a percentage of 57.5. Those prepared with 70° alcohol should contain 67% alcohol. Prepared with 80° alcohol, the percentage is 77.5, excepting in tinctures made from dry products like benzoin, tolu and guaiac. Laudanum should contain 29%; the saffron should have 57% moisture. The larger figures given do not hold for tinctures made from substances containing no moisture, such as resins and dry extracts. It would be well to adopt formulas showing the degree of dryness of the substances employed for preparing tinctures. The Codex should prescribe the use of ground glass or paraffined stoppers, in order to prevent tinctures from losing alcohol by evaporation.

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(1c—172½)

**Sensory Stimulation by Saturated Monohydric Alcohols.**

*Marian Irwin, Am. J. Physiol., 60:151, March 1, 1922.*

This investigation deals with certain effects of alcohols, especially  
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with the question whether in a series of isomers branching of the chain determines the relative efficiency of the members of the series. The experiments were performed on *Allolobophora foetida*. The worm was placed on a table surrounded by a test solution, and allowed to crawl freely to the edge of the table and enter the solution. The reaction time (representing the time elapsing from the moment the prostomium of the worm enters the solution until it is withdrawn) was recorded. The efficiency of different members of the alcohols in the series was found by determining what concentrations bring about approximately the same reaction time. Methyl alcohol, ethyl alcohol, n. butyl alcohol, n. amyl alcohol, isoamyl alcohol and tertiary amyl alcohol were used. The tabulated results show the efficiency of alcohols at the given concentrations to be as follows: methyl < ethyl < tertiary amyl < n. butyl < iso-amyl < n. amyl. The same order was obtained when the ability to bring about cessation of muscular activity was taken as the criterion of the efficiency of the alcohol.

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(1c—173)

**The Fate of Methyl Alcohol and Isopropyl Alcohol.**

*Julius Pohl, Biochem. Ztschr., 127:66, Berlin, Feb. 28, 1922.*

Experiments showed that daily doses of even 3 gm. methyl alcohol administered to dogs weighing up to 14 kg. lead to increased formic acid elimination and retention of methyl alcohol. This observation is of importance because in the northern European countries a so-called sulphite ethyl alcohol, containing up to 2% methyl alcohol, is marketed in great quantities as a substitute for beverage ethyl alcohol. Such an alcohol is fit only for technical uses. Regarding isopropyl alcohol it should be mentioned that its toxic properties are considered the same as those of ethyl alcohol. It may be obtained easily from calcium carbide over acetylene, acetaldehyd, acetic acid and acetone by a catalytic reducing process from the latter. The experiments show that small doses of isopropyl alcohol, which cause no symptoms of intoxication, are used up 80%. The administration of small amounts did not cause any growth disturbance nor any alteration in general condition. If the isopropyl alcohol at present produced in such large quantities could be freed from its unpleasant odorous bodies its use as a beverage in reasonable amounts would not be objectionable. Substances like sodium iodid, quinin, adrenalin, oxyphenylethylamin and histamin, which are ordinarily regarded as active in metabolism, could not be shown to possess a definite influence on alcoholic oxidation. Also, it was not possible to demonstrate an influence on albumin metabolism even with larger doses.

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(1c—174)

**The Effect of Beta Imidazolylethylmin (Histamin).**

*Paul Schenk, Arch. f. exper. Path. u. Pharmakol., 92:34, Leipsic, Feb. 28, 1922.*

Histamin has the opposite effect from that of adrenalin on the capillaries, bronchi, stomach, intestines, virgin uterus, pupils, coronary vessels, vessels of the lungs and bladder. Schenk first studied the effect of histamin on sugar mobilization in the liver. He used rabbits as  
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experimental animals and established the following facts: (1) Histamin does not inhibit the sugar-mobilization action of adrenalin but rather increases it. (2) Histamin itself has a slight sugar mobilization action. He found the same results in studying the effect of histamin on the frog liver, and on the increased formation of sugar in the liver caused by the giving of adrenalin. Therefore histamin, unlike ergotoxin, does not inhibit the sugar-mobilizing action of adrenalin. After the injection of 3—4 mg. of histamin, the capillary endoscope shows that the capillaries of the skin dilate, but it still remains an open question whether this is due to a direct paralysis of the constrictors of the capillaries, or to a passive dilatation of the capillary loops, as a result of active dilatation of the afferent arteries. From his observations, Schenk concludes that histamin decreases the excitability of the sympathetic with the exception of the stimulating actions of the sympathetic on glycogen formation. Anemia could not be produced in rabbits by the continued administration of histamin. The effect of histamin on heart action is slight. The frequency of the heart beat is increased, but its rhythm remains unaffected.

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**The Reputed Vesicating Properties of the Granary Weevil,  
Calendra granaria.**

*William A. Riley, New Orleans M. & S. J., 74:679, April, 1922.*

There is prevalent among entomologists and medical men interested in the subject the idea that the granary weevil, *Calendra granaria*, possesses vesicating properties comparable to those of the true cantharides. It has also been suggested that they are responsible for some of the instances of poison flour. At the writer's suggestion a graduate student has undertaken experiments, checking over the work thoroughly by use of commercial cantharides. Her results will be published elsewhere in detail, but up to this time she has failed wholly in her efforts to demonstrate the vesicating effect of calendras. Without exception the control preparation of mylabridae, the Chinese blister beetle which she used, caused vesication and since she used all of the standard solvents of cantharidin, it seems clearly established that *Calendra granaria* does not possess this substance. In addition to these attempts to produce blisters, isotonic solutions of the dried calendras in salt solution were injected into rats and mice. Check experiments were performed with a clear salt solution of the same concentration, and with a solution of mylabridae prepared exactly as were those of calendras. The animals injected with the calendras and the salt solution were unharmed. All of the check rats injected with mylabridae solution died within two hours after injection. Feeding experiments were likewise tried upon mice, rats, frogs, chickens, and rabbits. The results were all negative. In order to obtain further information regarding the possible effects of the granary weevil, the writer ingested a grain (.06 gram) of the powdered calendra beetle, the dosage usually given internally for cantharides and one quite sufficient to cause definite results with that drug. Although the powder was taken on an empty stomach, there were none of the painful or disagreeable symptoms that would have followed the ingestion of the true cantharides. In view of the fact that the related rice beetle *Calendra oryzac* is very common in the Southern United States, the detailed

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experiments on vesication were also extended to this species because of the possibility of a confusion of this species with *C. granaria*. The results were altogether negative.

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**The Influence of Purgatives upon Blood Concentration.**

*Frank P. Underhill and Louis Errico, J. Pharmacol. & Exper. Therap., 19:135, March, 1922.*

Magnesium sulphate (Epsom salt), in experiments on dogs, produced a distinct rise in the hemoglobin which reached its maximum in about the second hour and returned to normal two and one-half hours after administration. The same result was obtained with sodium sulphate and sodium and potassium tartrate (Rochelle salt) except that the return to normal was about half an hour sooner. The hemoglobin content has never gone above 120% of the normal, the maximum having ranged between 114 and 120% of the normal. By ill-advised use of purgatives it is quite apparent that a blood concentrated to some extent, and yet not sufficiently to be dangerous, may reach a dangerous concentration by the added influence of the purgative. Such a factor may account in part for the collapse which at time follows the administration of a purgative. Castor oil and cascara sagrada produced no change whatever in the hemoglobin.

(1c—177)

**The Distribution Coefficients of the Diuretics and Narcotics and the Theory of Narcosis.**

*Giuseppe Aiello, Biochem. Ztschr., 124:192, Berlin, Nov. 21, 1921.*

Investigating the theory that the important element in narcosis is the solution of the neutral substances in the lipoids, experiments were recently conducted to determine (1) whether the diuretics are lipoid-soluble; (2) how the distribution coefficient acts between oil and water; and (3) what differences are found when water is exchanged for serum. Experience showed that obviously this change of water for serum could be extended to some narcotics. The method used was as follows: 50 c. c. 1% caffein solution was thoroughly mixed with 50 c. c. purest olive oil in a thick-walled bottle of 300 c. c. capacity for two hours; this was left standing for six hours and then separated in a separating funnel and the amount of caffein taken up by the oil was determined: the distribution coefficient between oil and water was 0.53 for the caffein, which distribution coefficient corresponds to that of some hypnotics. The same procedure was then followed as to serum and oil, in which a distribution coefficient of 0.18 was found for caffein. It is important to note that caffein is much more soluble in serum than in water.

The experimental tables show that the distribution coefficient of theophyllin dissolved in water is half that of the oil-serum system. The behavior of the true hypnotics trional and sulphonal is still more interesting: the distribution coefficient, 4.5, with trional falls to 0.27 in the oil-serum system; with sulphonal it falls from 1.11 to 0.21. These experiments show that another group of combinations, as excitants and diuretics of the caffein group, tested in a manner similar to that  
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employed with the hypnotics give values which at least closely resemble the values of the hypnotics, but that these also give other numerical values than those of the experiments in the oil and water system, with change of system and the approximation of the whole experiment to the possible conditions.

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**Mechanism of the Anesthetic Gases, Nitrous Oxid and Acetylene.**

*Hermann Wieland, Arch. Exper. f. Path. u. Pharmacol., 92:96, Leipsic, Feb. 28, 1922.*

Wieland shows that the action of nitrous oxid as an anesthetic is due to a lack of oxygen. This explains the well-known fact that when mixed with oxygen nitrous oxid is ineffective, but that when mixed with hydrogen it has an effect on frogs, as shown by his own experiments. This explains why this gas does not have any effect on an oxybiotic processes. This principle applied to experiments on ascarides, an isolated frog muscle and on excised frog heart, but the frequency of the beat of the frog heart is not effected directly by nitrous oxid. This gas is, therefore, not an anesthetic in the ordinary sense of the word. Since it is chemically indifferent in the body, its effect is due to its physical properties, particularly to its high solubility in water (the absorption coefficient for water at 5° C. is 1.0480); this gas is 50 times more soluble in water than nitrogen or hydrogen. If this theory is correct, then acetylene, which is just as soluble in water (absorption coefficient for water at 5°, 1.49) should have a narcotic action also.

Pure acetylene was used for all the experiments, for the impure gas is very toxic. Like nitrous oxid, acetylene has no effect on an oxybiotic process. Experiments on ascarides, on fermentation of sugar by yeast, on excised frog heart, and on paramecia, which had been kept for a long time in an atmosphere free of oxygen, showed the correctness of this theory. There was an anesthetic action: (1) on frogs. After a very short time, anesthetic action was perceptible; after twenty-four hours' action the frogs did not recover. Acetylene differs from nitrous oxid, in that it has an anesthetic action only in the presence of O<sub>2</sub>. (2) On white mice. The lower limit of effective concentration was 37% acetylene in air. With a concentration of 71% acetylene and 29% air, the mice remained alive after two hours. In a mixture of acetylene-oxygen, the fatal concentration was 85% acetylene and 15% oxygen. In general, the action of acetylene begins more quickly the greater the acetylene concentration and the less the oxygen tension. During anesthesia, the frequency of respiration and the temperature of the mice fall, and the total metabolism is decreased. If the acetylene is expelled by oxygen, the animal awakens very quickly. Acetylene brings about a condition which resembles hibernation. Just as in hibernation, the waking of the animal can be hastened by heating it. (3) On guinea pigs: The body temperature sinks during the anesthesia about 4°. (4) On rabbits: A mixture of 78% acetylene and 22% oxygen, corresponding to atmospheric air, causes a pronounced narcotism, during which the blood pressure rises to 140 mg. mercury in twenty-five minutes. (5) In man (experiments on himself) Wieland found that anesthesia begins twenty seconds at most after beginning

to inhale the gas, and in about three minutes is complete. Recovery was rapid after the gas was stopped. There was marked muscle rigidity during the anesthesia. All the experiments show that neither nitrous oxid nor acetylene has any effect on anoxybiotic processes, but that they have an anesthetic effect on higher animals and on man. The mechanism is as follows: Oxidation in the cerebrum is disturbed. It is certain that this phenomenon is not caused by a combination of the gas with the hemoglobin, but that it is physically combined with the blood on account of its high solubility in water. Both of these gases should be distinguished from the ordinary anesthetics with high lipid solubility. The coefficient of distribution,  $\text{ol} \div \text{H}_2\text{O}$ , for acetylene is 1.39, for nitrous oxid, 1.89; but their slight solubility in oil as shown above is of secondary importance. Their chief effect is due solely to their ready solubility in water.

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**Action of Stovain and Novocain on the Bulbar Centers.**

*Jean Canis, Paris méd., 12:205, March 11, 1922.*

The author has studied the effects of various substances on the functions of the bulbar centers, by injecting these through the atlido-occipital membrane. Particular attention was given to stovain and novocain, with a view to finding a means of treating the serious bulbar symptoms which sometimes develop in the course of spinal anesthesias. An animal which receives amounts somewhat higher than the normal lethal doses dies through paralysis of the respiratory centers. Stovain is decidedly more toxic in this respect than novocain. Stimulation of the central end of the vagus has no effect on the respiration at this stage, but if artificial breathing is resorted to, respiration reappears spontaneously, and stimulation of the vagus is followed by an acceleration of the respiratory rhythm. Although the respiratory centers are paralyzed, others such as the vasomotor and inhibitory cardiac centers are still functioning. When a quantity of the drug somewhat below the lethal dose is given to a dog, the respiratory centers are nevertheless affected, and a shock or sudden change of position may sometimes suffice to bring on fatal syncope. Under these conditions an intraspinal injection of caffeine proves effective against the syncope, provided the amount given does not exceed the usual lethal dose. Even when the respiratory centers are paralyzed, artificial breathing, sometimes prolonged for over one hour, may restore life.

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**Changes in Metabolism Caused by the Chronic Use of Morphin.**

*Fritz Hildebrandt, Arch. f. exper. Path. u. Pharmakol., 92:68, Leipsic, Feb. 28, 1922.*

Experiments of Reid Hunt on the toxicity of morphin in normal mice and rats, and ones that had been fed with thyroid gland, showed an increased toxicity after thyroid gland feeding. Hunt cannot explain this fact; he only suggests the hypothesis that as a result of the increased oxidation of fat caused by thyroid feeding, possibly the lipoids of the central nervous system are so changed, that toxins, for example, morphin, can penetrate them more readily. But it is also possible that, as with acetonitril, so also with morphin, catabolism is inhibited by

thyroid feeding, which must necessarily result in greater toxicity. Hildebrandt's experiments were designed to show whether in the catabolism of rats there is any relationship between the action of morphin and the function of the thyroid gland. All the experiments were made on rats which had been given a constant diet of 15 gm. bread and 15 gm. milk in twenty-four hours. The gas exchange ( $O_2$  intake and  $CO_2$  outgo) was determined with a modified E. Rolde's apparatus. In the normal animals the respiratory quotient three hours after feeding, was 0.85—0.9, and fell within the next few hours to 0.73—0.78; in the urine 0.13—0.15 nitrogen was excreted with a nitrogen intake of 0.22. Two animals were given 0.5 gm. thyroid tablets daily. On the second day the total metabolism rose, while the respiratory quotient fell to 0.66. On the seventh day the respiratory quotient rose, and at the same time more nitrogen appeared in the urine. This indicates that after the feeding of thyroid, metabolism increases, chiefly due to the increased oxidation of fat. Fifteen experiments on thyroidectomized animals gave uniform results, decrease of metabolism at first, and increased respiratory quotient with the amount of excreted nitrogen remaining the same. After about four weeks the metabolism returned to normal, and the respiratory quotient also showed normal values. In other words, in the beginning after thyroidectomy the total metabolism is decreased with a primary increase in the oxidation of carbohydrates. The effect of chronic morphin intoxication was also studied in 22 experiments. The findings which agreed in the different experiments are: (1) Decrease of metabolism with increased respiratory quotient, the highest figures being found after about fifteen days of morphin treatment. (2) In the terminal stage of morphin poisoning there is a sudden fall of weight with a considerable rise in total metabolism. Hildebrandt draws a comparison from the respiratory experiments on thyroidectomized animals: decrease of metabolism with primary increase in oxidation of carbohydrates in both conditions. He also points out 2 further analogies: (1) Decrease in the respiratory quotient in animals habituated to morphin after administration of thyroid substance. (2) Slight sensitiveness of animals accustomed to morphin to lack of oxygen; the same thing is true of thyroidectomized animals. These experiments were carried out on normal animals, thyroidectomized animals, and animals habituated to morphin, all kept under negative pressure. Animals fed with thyroid are more sensitive to morphin than normal animals (lethal dose for the former, 40—50 mg.; for the latter 50—60 mg.; while the lethal dose for thyroidectomized animals is 100 mg. morphin.)

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**A New Hypnotic: Phenylethylhydantoin.**

*Eugène Gelyna and Alfred Schwartz, Paris méd., 12: 162, Feb. 25, 1922.*

Phenylethylhydantoin is a synthetic product derived from urea. It differs from veronal and luminal by the substitution of hydantoin (glycolylurea) for malonylurea. Its sodium salt is soluble and can be injected hypodermically. From experiments on animals it seems that phenylethylhydantoin has a stronger hypnotic action than veronal while being less toxic than either veronal or luminal. Several cases are known where symptoms of intoxication appeared following the ingestion of  
(Sec. 1—Page 910)

about 50 cm. daily for several days. These symptoms consisted in an eruption resembling that of scarlet fever or measles, fever, pruritus, cyanosis and edematous swelling of the face. Two fatal cases are known, but it is doubtful whether they are to be attributed to phenylethylhydantoin. The authors themselves have seen no dangerous signs of intolerance following the administration of this drug which gave them better results than veronal or luminal in cases of simple insomnia due to mild febrile conditions or to psychoneuroses. No phenomena of intoxication were noted even after prolonged use. Phenylethylhydantoin acts a quarter of an hour after being ingested and the effect lasts twelve hours. There is no feeling of heaviness on waking. The effective dose ranges between 30 and 75 cm. in twenty-four hours.

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**Comparative Experiments on the Antiseptic Action of Some Chlorin Derivatives of Methane, Ethane and Ethylene.**

*Georg Joachimoglu, Biochem. Ztschr., 124:130, Berlin, Nov. 21, 1921.*

Experiments were conducted to determine the concentrations at which a certain amount of bacilli are killed after twenty-four hours at room temperature. As the antiseptic action of the tested watery solutions of the chlorin derivatives of methane, ethane and ethylene (dichlormethane, chloroform, tetrachlormethane, ethylenedichlorid, tetrachlorethane, pentachlorethane, hexachlorethane, dichlorethylene, trichlorethylene and tetrachlorethylene) is slight, the tests were made with the *Vibrio metschnikovii*, which is usually very sensitive to antiseptics; the colon bacillus was found to be too resistant. The experiments were conducted in the following way: a twenty-four hours' slanting agar culture was covered by *V. metschnikovii* in 2 c.c. physiologic saline solution and of this suspension 3 drops were put in the particular watery solution of the chlorin combination. The tubes were left to stand in the dark at room temperature. On the following day a loopful of the suspension was transferred to the agar slant, incubated for twenty-four hours and the result was read off: The concentrations in molecular weight which destroyed the *V. metschnikovii* were as follows: with dichlormethane, 0.1037; with chloroform, 0.04615; with tetrachlormethane, 0.00449; with ethylenedichlorid, 0.0455; with ethyldenechlorid, 0.0166; with tetrachlorethane, 0.00357; with pentachlorethane, 0.00064; with hexachlorethane, 0.00002243; with dichlorethylene, 0.00858; with trichlorethylene, 0.005372, and with tetrachlorethylene, 0.0002929. The antiseptic effect on *V. metschnikovii* of these combinations ranges in the following order: hexachlorethane, tetrachlorethylene, pentachlorethane, tetrachlormethane, ethylenedichlorid, trichlorethylene, dichlorethylene, ethyldenechlorid, tetrachlorethane, chloroform and dichlormethane.

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**Study of the Action of Adrenalin on the Vessels in Man.**

*B. Fornet, Arch. f. exper. Path. u. Pharmakol., 92: 165, Leipsic, Feb. 28, 1922.*

The use of adrenal extract for diagnostic and therapeutic purposes has become increasingly important in recent years. It has been given almost entirely by subcutaneous injection. In view of the complicated

conditions of absorption and the possibilities of destruction and oxidation, which interfere with the complete action of adrenalin when given subcutaneously, it has long been assumed that the effect is produced by only a part of the adrenalin. Since the animal experiments of Straub-Ritzmann and Kretschmer have shown that 94% of the adrenalin given subcutaneously is destroyed or oxidized, and only 6% takes effect, this has been held to be true for the human body also. What far-reaching consequences may result from this, and how necessary it is that these results should be tested on man, is illustrated by a case reported by Fischer, in which he was called upon to pass judgment from a medico-legal point of view.

A patient was given 10 c.c. of a 1% adrenalin solution subcutaneously, and died in six minutes. Fischer mentions the above experiments and says that judging from the experiments of Ritzmann, 6% of the 10 mg. adrenalin reached the circulation. This amounts to the minimum dose of 0.6 mg. For this reason he says in his legal opinion that it is not certain that death was caused by adrenalin intoxication.

Fornet evaluates the effect of adrenalin given subcutaneously and intravenously by measuring the blood pressure. By comparing the blood pressure curves when adrenalin is injected subcutaneously and intravenously, he showed that it is not true that 96% of the adrenalin given is destroyed in the subcutaneous tissues. His calculations show that at least 42% of the adrenalin injected subcutaneously is absorbed. Nor is the adrenalin destroyed immediately in the blood, as shown by experiments on the ligated extremity. When adrenalin was injected intravenously into a section of the vein, there was an immediate rise in arterial pressure. The same method of experiment with subcutaneous injection showed the falseness of the hypothesis that adrenalin injected subcutaneously is destroyed within twenty minutes. Finally he showed that hyperemia caused by heat hastens the absorption of adrenalin so that the rise in blood pressure is violent, while the opposite result is brought about by cold. From all his experiments, Fornet concludes that true sensitiveness to adrenalin can only be tested by intravenous injection.

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**A Note on Adrenalin Hyperglycemia in Man.**

*Henry L. Ulrich and Harold Rypins, J. Pharmacol. & Exper. Ther., 19: 215, April, 1922.*

A concentration of the blood following adrenalin as observed in dogs was not paralleled in man, the maximum intravenous dosage being employed. The mechanism of adrenalin hyperglycemia in man could not be explained on the basis of a change in blood concentration due to the adrenalin, but occurred independently of such a change. The maximum intravenous dosage of adrenalin in man was approximately 0.33 c.c. of a 1:1000 solution in a 70 kilo man, which corresponded to about one-one hundred and eightieth of the physiologic intravenous dose per kilo in dogs. Intravenous adrenalin caused a wide and inconsistent fluctuation in the concentration of blood creatinin and blood urea nitrogen.

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**Perfusion of the Medulla of the Terrapin (*Pseudomys Troostii*) with Adrenalin.**

*W. J. R. Heinekamp, J. Pharmacol. & Exper. Therap., 19: 131, March, 1922.*

The present experiments were prompted by the statement of Bush that epinephrin does not seem to exert a registerable influence on the cardio-inhibitory center of the striped turtle. After removing the plastron, the cord was cut as low down as possible, well within the carapace, then all structures other than the two carotid arteries and vagus nerves were severed, the nerves alone being the only connectives between the body and the head, since both carotids were tied off and a cannula inserted into one. Ventricular rhythm was recorded by attaching the apex to a recording lever. The yellow bellied terrapin was used exclusively, it having been found that the map turtle did not respond to vagus stimulation. Ringer's solution was used as a diluent and for washing out the medulla before and after the drugs. The solutions used were prepared from the tablet adrenalin of Parke, Davis and Company, and made up immediately before perfusion. It was found that in concentration of 1:10,000, oxidation was evident to the eye in about twenty minutes in an alkaline solution such as Ringer's. Partial or complete inhibition was obtained in about 80% of the experiments. With dilute solutions as 1:100,000, irregular slowing was produced. With 1:50,000 adrenalin, complete inhibition was produced in a number of cases; slowing became evident in three and one-half minutes and complete inhibition was evident in five and one-third minutes respectively. Total inhibition, however, did not follow.

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**Energometric Experiments on the Effect of Adrenalin on the Circulation with Observations on the Wall Pressure of the Arteries.**

*A. Hotz, Dcutsch. Arch. f. klin. Med., 138: 257, Leipsic, Feb. 21, 1922.*

The best known and most important practical effect of adrenalin is the increase of the blood pressure, caused by a narrowing of the smaller vessels due to an effect on the vessel wall itself. There is also a direct and powerful stimulation of the heart. Steinach and Kahn maintain that there is probably also a vasoconstrictor effect on the capillaries. The vessels supplied by the splanchnic nerve are involved to the greatest degree, including the vessels of the intestines, liver and kidney, while the vessels of the brain, retina, lungs, extremities and the coronary vessels are little if at all affected. The present view is that adrenalin dilates the coronary vessels.

The results of animal experiment agree very well with those of clinical observation. The author attempted to analyze further the clinical effects of adrenalin by experiments on children. The effect of adrenalin was most marked ten to thirty minutes after injection and lasted up to one hour, the pulse volume being increased. In 5 cases the pressure dropped after 25-85 minutes below the reading found at the beginning of the experiments.

Bayer claims that this is not always due to relaxation of the  
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vessels from exhaustion because Kretschmer could produce increase of pressure to the same degree by continued injections. He favors the theory of simultaneous stimulation of the dilator elements which is manifested only after the vasoconstrictor effect has been abolished. This resembles the effect of coincident electric stimulation of the vasoconstrictors and dilators. The average increase of total energy was about 48% while the actual work accomplished amounted to about 30%.

Total energy consists of net energy and wall pressure. The latter amounts to about 1% of the total energy in the healthy child. In adults the mean diastolic pressure was 95 cm. H<sub>2</sub>O, the mean systolic pressure 125 cm. H<sub>2</sub>O. The mean wall pressure was 30 cm. H<sub>2</sub>O or 22 mm. Hg. The same values were obtained in children.

The increase in the pulse volume of the brachial artery after adrenalin is accompanied by a drop in diastolic pressure. This is probably due to passive dilatation of the artery with resulting increased flow of the right heart. The drop in diastolic pressure in the brachial artery indicates that there is increased flow away from this artery. This is perhaps the most plausible explanation, on the assumption of a purely passive dilatation of the artery. Possibly, but not necessarily, vasodilatation is also an active process.

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**The Physiologic Action of Metallic Ammonia Bases and Related Combinations.**

*Ad. Oswald, Biochem. Ztschr., 127:156, Berlin, Feb. 28, 1922.*

Metallic ammonia bases attack the motor elements of the nervous system in warm and cold blooded animals and produce increased irritability, spasm and paralysis. Quantitative differences are observed in the individual bases. In the case of platinum, cobalt, chromium and rhodium combinations the action increased with an increase in the number of ammonia molecules. The metallic component is without influence. The researches were extended by investigations of the combinations of other metals with ammonia and such with ammonia derivatives, aliphatic amines, cyclic bases and also ammonia residues that no longer contained ammonia. The experimental animals were frogs, white mice and white rats. There were examined compounds of cobalt, nickel and bromine with ammonia as well as combinations of these metals with diethylendiamin, pyridin and phenanthrolin. Further, metallic oxalate and metallic malonate compounds were investigated. The substances were administered subcutaneously.

Metallic ammonia bases as well as compounds of a metal with substituted ammonia show the typical properties of the linked radicals, i.e., the action of ammonia or that of the substituted ammonia. Both are identical and act on the motor centers first by increased excitation and then by paralysis. This is observable even when the metallic complexes do not dissociate in aqueous solution and, therefore, leave the organism undissociated, like tridipyridyl ferrobromide and triphenanthrolin ferrobromide. All the physiologic properties appear to be referable to a few fundamental types. Such types are the methane, benzene and ammonia types. Metallic ammonia bases, ammonia derivatives, and pyridin and phenanthrolin compounds, behave like the ammonia type.

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**Biologic Reactions of Arsphenamin. I. The Mechanism of Its Agglutinative Action on Red Blood Cells in Vitro.**

*Jean Oliver and Ethel Douglas, J. Pharmacol. & Exper. Therap., 19: 187, March, 1922.*

Arsphenamin had a fairly constant agglutinating titer for red blood cells. The cells of different species varied somewhat in their agglutinability. Human cells were most strongly acted upon, chicken cells the least. There was a drop in the titer of salt dilutions of arsphenamin as they stood in the open air. Arsphenamin was adsorbed by red cells, but no agglutination occurred except in the presence of an electrolyte. A physical change in the degree of dispersion of arsphenamin resulted when an electrolyte was added to arsphenamin in solution. It is suggested that the action of electrolytes in the process of agglutination is due to this action on the adsorbed arsphenamin of the sensitized cells.

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**Biologic Reactions of Arsphenamin. II. The Protective Action of Hydrophilic Colloids on the Agglutination of Red Blood Cells by Arsphenamin.**

*Jean Oliver and So Sabro Yamada, J. Pharmacol. & Exper. Therap., 19: 199, March, 1922.*

The agglutination of red cells by arsphenamin was inhibited by many hydrophylic colloids. The protective power of certain of these substances studied corresponded roughly with their efficiency as expressed by the gold number. Both phases of the process of agglutination are affected in this inhibition, the union of the arsphenamin with the red cells and the action of the electrolyte on the arsphenamin. Adsorption phenomena between the protective colloid and the arsphenamin will explain the lack of reaction of the latter with both the other elements, cells and electrolyte, which is necessary for agglutination.

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**Cholin as a Hormone of Intestinal Movement. Peristalsis. VI. Experimental Therapy of Gastro-Intestinal Paralysis Following Peritonitis and Laparotomy.**

*K. Arai, Pflüger's Arch. f. d. ges. Physiol., 193: 359, Berlin, Feb. 9, 1922.*

In cats, intraperitoneal injection of 0.05 c.c. Lugol's solution (2%) per kilo of body weight produces typical serofibrinous peritonitis with all characteristic changes of the peritoneum and a very regular course. It reaches its maximum in two or three days after the injection and heals in the course of a week, leaving slight adhesions. The clinical phenomena include distinct weakening of gastric and intestinal movements, as may be observed by radiologic examination. The passage of food through the stomach and small intestine is greatly delayed, the passage through the proximal colonic segment is accelerated and evacuation is greatly affected. This paralysis of the alimentary canal is most marked from 24 to 48 hours after injection and has almost disappeared after 120 hours.

These phenomena may be completely abolished by intravenous administration of cholin chlorid (10 mg. per kilo of body weight) at the height of gastro-intestinal paralysis. Gastric and intestinal peristalsis increases, and the contents traverse the alimentary canal more rapidly, the digestive process proceeding in a normal manner. The movements of the large intestine are also stimulated and normal evacuation occurs. During such peritonitis the cat's intestine contains the normal amount of cholin. The irritability of the isolated living large or small intestine of peritonitic animals is the same under cholin administration as that of normal animal organs.

Laporatomy with drawing forward of individual sections of the gastro-intestinal tract and manipulation in the air produces typical post-operative gastro-intestinal paralysis in cats, which corresponds entirely to that observable in man. This paralysis is also abolished by injection of 0.10 mg. cholin chlorid (about 5 mg. per kilo); again, gastro-intestinal peristalsis is increased and the passage of the food through the alimentary canal is accelerated. Doses of 15 mg. per kilo produce marked stimulation in the region of the proximal and distal colon and evacuation of the large intestine. This could be demonstrated by filling the previously empty large intestine with a contrast medium. In this case, too, the cholin content of the small intestine shows no variation from the normal. The isolated large intestine of cats, rabbits and apes can be stimulated by cholin the same as the small intestine. The various sections of the large intestine show the same behavior under this treatment. No injury to the experimental animals (cats) was observed with doses up to 15 mg. per kilo, and even 25 mg. are tolerated well; 30 mg. produce reversible arrest of respiration and 35 mg. cause death (intravenous injection). For mice the lethal dose is 0.79 mg. per kilo subcutaneously. If the cholin solution is introduced very slowly, 1.3 to 2.6 mg. per kilo per minute, it is possible to inject about double the lethal dose, namely, 63.8 to 67.8 mg. per kilo. If the rapidity of injection be reduced still further, or the dilution of the solution be increased, the lethality is diminished further and 0.8 to 0.9 mg. per kilo per minute is almost nonpoisonous and is tolerated for hours without harm. Contrary to Werner's statements, the toxicity of cholin borate (enzytol) depends entirely on the cholin content and is not any less than that of the other cholin salts (10 gm. enzytol correspond to about 8.45 gm. cholin chlorid). These experimental determinations, supported by curves and roentgenographs, supply a safe basis for the therapeutic use of cholin in human gastro-intestinal paralysis.

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**The Relative Toxicity of the Halids and Certain Other Anions.**

*A. T. Cameron and M. S. Hollenberg, J. Gen. Physiol., 4:411, March 20, 1922.*

In order to determine the survival periods of frog heart and gastrocnemius-sciatic preparations (*Rana pipiens*) immersed in modified Locke solutions in which varying amounts of sodium chlorid were replaced by the corresponding molecular concentrations of the sodium salts of the anions fluorid, bromid, iodid, chlorate, iodate and nitrate, (Sec. 1—Page 916)

in each set of experiments the solutions were made up with freshly distilled water, and the preparations, dissected as quickly as possible, were immersed in them in shallow vessels, so that the oxygen supply could be regarded as sufficient. The volume of solution, compared to volume of tissue, was large. From time to time the preparations were observed and tested. The times were noted at which the hearts ceased to respond to electric stimulation and the muscles ceased to respond to such stimulation applied (a) directly, and (b) through their nerves. In all cases it was observed that nerve tissue died shortly before the death of the corresponding muscle. It was also noted in the experiments that a difference of a few degrees of temperature had a marked effect on the duration of life of the muscle-nerve preparations, in whatever solutions they were immersed; the authors therefore maintained for the experimental procedures a fairly constant temperature of 5° C. The tabulated results show that the period of survival decreases with increase of temperature in all solutions. The authors attribute this phenomenon to the combined effect of temperature per se, and of temperature in increasing the toxic effect of the foreign ion. It was also observed that introduction of any foreign ion into the Locke solution, under constant temperature conditions, decreases the survival period. This is due to toxicity of the foreign ion. The greatest relative toxic effects were produced by an initial slight replacement of chlorid ions. The experiments also revealed a distinct difference of action in solutions in which 2 and 3% of chlorid ion was replaced by iodid and nitrate. For the greater replacement, iodid was more toxic than nitrate; for the lesser, iodid was less toxic. For Locke solutions in which more than 5% of chlorid was replaced by the corresponding molecular concentration of the foreign ion, the toxicity is in the descending order:  $F > IO_3 > I > NO_3 > ClO_3 > Br > Cl$ . When less than 2% of the chlorid is replaced, the order is  $IO_3 > NO_3 > I > Br > Cl$ .

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**The Effect of Iodized Albumin on the Metamorphosis of Frog Larvas.**

*I. Abelin, Pflügers Arch. f. d. ges. Physiol., 193:624, Berlin, Feb. 22, 1922.*

The acceleration of the metamorphosis of frogs by thyroid substance is not a strictly specific action, since it can be produced by other combinations (di-iodotyrosin, di-iodotyrannin, iodo-albacid). Thyroid gland devoid of iordin produced no effect. Tests were made with iodized gelatin, a substance relatively free from cyclic amino-acids, and with iodocasein, which contains several such combinations. Iodized gelatin was absolutely ineffective, while iodized casein was found to somewhat accelerate the absorption of the tail, but did not produce any typical acceleration of the metamorphosis. However, Jensen has obtained positive results with iodocasein. These varying results can be explained by a different chemical structure of the iodized albumins used. Its effect upon the metamorphosis of the larvas depends mainly upon the constitution of the iodized molecule. The marked differences in the structure of the albumin bodies and the variable iodization, depending on the relative amounts of iordin and albumin, the duration of the iodization,

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the reaction of the medium, produce different combinations with each attempt, and these naturally exert different effects. The action of iodized albumin bodies upon the metamorphosis of pollywogs depends neither upon the percentage of iodin nor upon the albuminous nature of the active substance.

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**The Effect of Iodin and Iodothyrin on the Larvas of Salamanders. I. The Effect of Iodothyrin and Iodin on the Metamorphosis of Ambystoma Maculatum.**

*E. Uhlenhuth, Endocrinology, 6:102, Jan., 1922.*

These experiments reveal that the administration of inorganic iodin, which produces precocious metamorphosis in tadpoles has not the slightest effect on the metamorphosis of salamander larvas, although iodothyarin causes prompt metamorphosis in the latter just as it does in tadpoles. In salamanders the thyroid hormone is not excreted during the greater part of the larval period, while in tadpoles excretion of the thyroid hormone begins early in larval life. This explains why the administration of an excess of inorganic iodin can produce precocious metamorphosis in tadpoles while it is completely ineffective in the larvas of salamanders. In order to cause metamorphosis, iodin must combine with the substances forming the nucleus of the thyroid hormone, and the rate of hormone excretion must increase with the increase of iodin available. In salamanders the rate of hormone excretion is not influenced by an excess of iodin, but depends on the action of a particular "releasing mechanism". There is at present no fact known, which would prove that inorganic iodin as such can function as a hormone. Two tables and a complete bibliography are given.

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**The Dependence of the Bactericidal Effect of the Alkaloids of Quinin on Alkalinity.**

*L. Michaelis, Klin. Wchnschr., 1:321, Berlin, Feb. 11, 1922.*

Morgenroth decided from the inconstancy of the findings that one could not deduce the action of disinfectants *in vivo* from the result obtained *in vitro*. The reason for this inconstancy is certainly complex but Michaelis has worked on one of the factors, namely, the alkalinity of the solution. J. Traube titrated the alkanity but Michaelis determined the pH as a simpler method.

The effects of the alkaloids were tested on the *Staphylococcus pyogenes aureus* both on agar plates and in bouillon cultures. It was shown that the disinfectant qualities of all the derivatives of quinin contained in a given quantity of alkaloid depended on the pH, and the more alkaline the solution, the stronger the effect. The limits, 7.0-7.5, showed that the slightest change of pH had a powerful effect. The alkalinity of the acidified inflammatory fluids and even of the blood is less than that necessary for the optimum effect of the alkaloids of quinin. It is necessary to employ alkaloids which have the same effect as the derivatives of quinin but which are weaker bases.

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**The Action of Salicylates on the Uterus.**

*J. W. C. Gunn and Morris Goldberg, J. Pharmacol. & Exper. Ther., 19:207, April, 1922.*

The movements of the isolated uterus were recorded by suspension in oxygenated Locke's solution in an apparatus similar to that of Dale and Laidlaw. When the movements became regular, or, if they were absent when the tone became constant, measured amounts of a warm solution of sodium salicylate in Locke's solution were added and the effects recorded. In most of the experiments the temperature of Locke's solution was kept at 40°, which corresponds to the pyrexia of rheumatic fever. The results showed that salicylate of soda in sufficient quantity stimulated the uterus, as evidenced by an increase of the tone or of the frequency or extent of its movements. The necessary concentration varied slightly, but 1 in 1000 was always effective. This was as a rule sufficient to induce rhythmical movements in a previous quiescent uterus, but in 2 experiments it produced a single powerful contraction of short duration but no regular movements. In most experiments 1 in 2000 had some stimulant action, and in one it caused the appearance of rhythmical movements. Lesser strengths had a slight stimulating action or none at all. One in 500 sodium salicylate produced primary stimulation, then depression. All these effects were reversible as the uterus returned to its previous state of movement and tone when the experimental solution was again replaced by Locke's solution. The same results were obtained on the pregnant and nonpregnant uterus of the cat, rabbit, guinea-pig and rat. The action is therefore presumably directly on the muscle, as it is independent of the predominant action of the inferior mesenteric nerves. The movements of the uterus *in situ* were recorded with Cushny's myocardiograph. The salicylate of sodium dissolved in warm saline solution was injected into the jugular vein. Twenty-one experiments were performed on the pregnant and nonpregnant rabbit and guinea-pig, the pregnant rat and the nonpregnant cat. In 2 cases a slight but undoubtedly stimulation was seen after doses of 20 mg. per kilo, and progressively increasing effects after larger doses. Subsequent experiments showed that any effects with such small doses were quite exceptional. In the later experiments 50, 100 or even 200 mg. per kilo was the initial dose. In more than a third of the experiments, salicylates had no effects on the uterus. In the remainder there was an increase in the rate or the amplitude of the movements. The stimulation did not usually last for long, in some not longer than the duration of the injection, in others five or ten minutes. It was particularly noticeable that in some animals that had received as much as 300 or 400 mg. per kilo in divided doses, the movements of the uterus a few minutes after the last injection were little if any more active than before any salicylate had been given.

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**The Effects of Primary Sodium Phosphate upon the Energy Capacity of the Human Body.**

*Herbert Herxheimer, Klin. Wchnschr., 1:480, Berlin, March 4, 1922.*

Induced by Embden's experiments with phosphoric acid in its  
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effect upon muscular activity, Herxheimer studied the effects of primary sodium phosphate ( $\text{Na H}_2\text{PO}_4$ ) upon muscular activity during a gymnastic police course. The participants engaged daily for three or four hours in gymnastic exercises, swimming, light and heavy athletic sports. One group was given 3 gm. primary sodium phosphate (in aqueous solution) daily, and a second group served as controls. The most remarkable result was an increase in weight which became apparent soon after the first administration of phosphate; after 5 weeks the average difference in weight between the two groups reached its maximum (670 gm.). On account of the severe physical exertion, this increase in weight cannot be ascribed to deposit of fat. If accumulation of water (hydro-pigenous action of the salt) had been responsible, the subjects would have lost weight immediately upon discontinuing the phosphate, but such a loss did not occur. There is, then, evidence that the sodium phosphate was absorbed by the skeletal and muscular structures.

The increase in musculature could be determined by measurements; there was an average increase of 0.23 cm. in the measurements of the thigh, and of 0.11 cm. of the upper arm. The effects upon the energy capacity were determined by comparing typical endurance performances of members of the two groups, for instance, the lifting of weights, running a distance of 3000 meters, and dumb-bell exercises. In all cases the results indicated the superiority of the phosphate group. Some of the members of the phosphate group (40%) declared that they were less tired and their general condition was much better; only a few complained of mild transitory disturbances.

The author concludes that daily administration of primary sodium phosphate causes a considerable increase in weight, probably of the skeleton and musculature, and increased energy capacity of the body, which can be determined by actual measurements. This effect might be attributed to increased regeneration of the lactacidogen of the muscles, which constitutes the energy factor of muscular activity.

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**Increase of Allyl Isosulphocyanate in Black Mustard Produced by Sulphur.**

*E. Maurin, Bull. d. sc. pharmacol., 29:76, Paris, Feb., 1922.*

As a fertilizer, sulphur has a threefold action. It promotes the assimilation of nitrogen; by transformation to sulphate it favors absorption of potassium, iron, aluminium and manganese; and it increases chlorophyll function and the fixation of atmospheric oxygen. In testing the effect of flowers of sulphur on black mustard, using 10 gm. sulphur per square meter, it was found that plant growth and seed crops were much increased. The yield of allyl isosulphocyanate was 11% greater in seeds derived from the plants so fertilized. The vegetable cell, therefore, seems more capable than the animal cell of synthesizing complex sulphur compounds from oxids of mineral sulphur. These facts are of interest to those who cultivate mustard for food or therapeutic uses.

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**The Influence of the Solar Rays on Belladonna and the Formation of Alkaloids in Its Leaves.**

*A. Goris and H. Deluard, Bull. d. sc. pharmacol., 29:74, Paris, Feb., 1922.*

The conditions of soil and humidity were made as uniform as possible in the experiments undertaken. In leaves exposed to the sun during growth the alkaloids of the first crop were present in the proportion of 0.65 gm. per 100 gm. leaves. The proportion in the second crop was 0.52 gm. to 100 gm. leaves. In plants at first shaded, then exposed to the sun, 0.42 gm. alkaloids were obtained per 100 gm. leaves. In leaves shaded during growth, the alkaloid yield was 0.39 gm. per 100 gm. leaves. Young plants exposed to the sun gave 2 crops in three months; shaded plants yielded but 1 crop. Sunned plants yielded 15 gm. dry leaves per plant, shaded plants giving but 9 gm. leaves per plant. The total crop obtained from sunned plants was 3 or 4 times as great as that gathered from plants kept in the shade. A plant exposed to the sun gives 7 to 8 times the quantity of alkaloids furnished by a shaded plant. Plant for plant, the yield of dry extract was sometimes about the same for sunned and shaded leaves but the yield of the single or total crop was much greater in the sunned plants, and the quantity of alkaloids in the extracts derived from these was greater.

(1c—199)

(1c—199)

**The Glucosids of Strophanthus.**

*M. Tiffeneau, Bull. d. sc. pharmacol., 29:68, Paris, Feb., 1922.*

There are several different species of strophanthus and much confusion exists in the use of strophanthus glucosids. The seeds are often not identified when collected or when appearing later on the market and chemists usually pay no attention to their origin. Pharmacists often neglect to state whether a given strophanthin is crystalline or amorphous, manufacturers do not discriminate and national usage is not uniform. The official plant in France is *Strophanthus hispidus*; in England and Germany, *S. Kombe* and *S. gratus*. Strophanthins have no official status in these countries. On the contrary, *S. Kombe* and the amorphous strophanthin extracted from it are official in the United States Pharmacopeia. Ouabian and the different strophanthins are compared in a differential table. It is admitted that ouabain is a distinct drug entity. Practically, the confusion is somewhat reduced by the fact that the only strophanthus glucosids marketed are crystallized ouabain, derived from *S. gratus*, and amorphous strophanthin K, obtained from *S. Kombe*. The description in the French Codex of 1908 and supplement of 1919 is artificial and inexact. The strophanthin of *S. hispidus* should not be included in the next Codex. Crystallized strophanthin K, obtained from *S. Kombe*, is of no commercial importance. Moreover, it is about one and one-half times as toxic as ouabain or amorphous strophanthin of *S. Kombe*. The question whether the amorphous strophanthin of *S. Kombe* should be included in the next Codex ought to be carefully examined. In view of the fact that the polarization and physiologic tests are artificial and variable, precise definitions should be made if the drug is so included. It is by

no means indispensable. Without rejecting amorphous strophanthin, it appears desirable to substitute for it crystallized ouabain, which is more fixed and stable. *(To be Continued)*

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(1c—200)

**Detoxicating Effect of Spinach Secretin Solution on Strophanthin.**

*K. Miyadera, Deutsch. med. Wochenschr., 48:313, Berlin, March 10, 1922.*

Bürgi performed experiments to determine the protective effect of rice-bran preparation (orypan) on the paralyzing effect of morphin on the breathing center. Miyadera performed experiments on the exposed frog's heart with a mixture of secretin solution (a spinach preparation containing vitamin) and strophanthin. He showed that the systole of the heart was distinctly prolonged.

This proves that the secretin solution neutralizes the toxic effect of solutions of strophanthin.

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**Tetralin in the Urine.**

*W. Röckemann, Arch. f. exper. Path u. Pharmakol., 92:52., Leipzig, Feb. 28, 1922.*

Many articles have appeared in the medical press on the bad effects on the human body of chemical substitutes used during the war. Tetralin (tetrohydronaphthalin) is in a certain sense a substitute, as it is used in place of turpentine, one of the chief constituents of floor polish; and thus it is introduced into the household and hospital. Tetralin itself is a hydrated napthalin of the formula  $C_{10}H_{12}$ , a fluid as clear as water with a boiling point of 205° to 208° C., and which becomes solid at -30°. As it is very volatile it enters the human body chiefly with the respired air. There is a strong odor on entering a freshly polished room. After breathing tetralin, the urine becomes olive green and gives a strong Tollen's test, (with naptha resorcin and HCl, corresponding to an increased secretion of phenylglycuronic acid. In hospital wards injury of the kidney from floor polish has been observed. Experimentally in rabbits and dogs, blood has appeared in the urine after feeding tetralin. In larger doses it has an injurious effect on the kidneys. In dogs it also causes diarrhea. After taking tetralin, the urine gives a strong diazo-reaction. Tetralin has the same reaction as naphthalin in the urine, namely, the ethereal extract of urine mixed with calcium chlorid and HCl, and shaken up with a 1% resorcin solution gives a cherry-red color. Urine containing tetralin gives the following characteristic reaction: The acid urine mixed with sodium nitrite solution gives a green color. The reacting body seems to be a special glycuronic acid. In order to test the nature of tetralin excretion, large amounts of this body were fed to rabbits and dogs, and the product of catabolism was isolated. In addition to other paired glycuronic acids, in rabbits ac-betatetralol, and in dogs ac-alphatetralol were paired with glycuronic acid. In dogs' urine naphthalin (hydronaphthalin) is formed from tetralol by the splitting off of water in the animal body. Beta-tetralol rotates to the left, crystallizes as a picrate, and also passes into dihydronaphthalin by the splitting off of water.

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**Six Cases of Acute Arsenic Poisoning.**

*J. S. Hesser, Hygiea, 84:176, Stockholm, March 16, 1922.*

Six children (3 boys and 3 girls) having found a glass bottle containing a white powder tasted it and were poisoned by the contents. The symptoms began one-half hour after they had tasted the powder and were characteristic of arsenic poisoning. The general condition was very bad, signs of gastro-intestinal irritation being nausea, vomiting, diarrhea and symptoms of colitis with mucus in the stools. Five of the children had albumin in the urine and a sediment with white blood-corpuscles and granulated cylinders. Five also had acetonuria with positive Legal's reaction, and 3 had positive Gerhardt's reaction. This acetonuria, which is not mentioned in text-books, is considered by the author to be hunger acidosis, as for three days the children had been fasting. Another symptom not mentioned in literature is the frequency of the pulse.

All the patients recovered. This poisoning has to be considered as light although the quantity of arsenic trioxid may have been 25 cg. Lethal dose of adults, 0.10-0.20 gm. The fortunate result must be ascribed to prompt treatment (milk, excitation of vomiting and washing out of the stomachs contents). The arsenic had probably been used for horses and had been provided, without doubt, by a circulating agent or commercial traveler. In any event the law regulating the sale of poisons should be more strictly enforced in order to avoid such dangerous accidents.

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**Relation Between the Suprarenal Capsules and Morphine Poisoning.**

*Juan T. Lewis, Rev. Asoc. médica argentina (Biol. Sect.), 34: 1104, Buenos Aires, Nov., 1921.*

It has been observed that rats whose suprarenals have been extirpated exhibit great sensitivity to morphin. On the basis of investigations on dogs, Lewis cannot draw definite conclusions, as so far it has not been possible to produce chronic suprarenal insufficiency. Operations performed by other authors on dogs anesthetized with chloral and morphin, intravenously, produced marked Cheyne-Stokes respiration and no excitability of the cerebral cortex; with a strong faradic current Lewis produced excitation in the case of a dog which was dying, and which had an arterial pressure of only 2 cm. Hg. Three dogs operated on under chloral and morphin revealed great depression afterward, as compared with those anesthetized with ether; all of them died from twelve to fifteen hours after operation.

Another investigation was made by ligating both lumbocapsular veins and administering chloral and morphin intraperitoneally. All the animals died in a few hours. Those operated on under ether anesthesia survived, presenting a very healthy appearance after several weeks. As morphin, even in anesthetic doses, shortens the life of de-capsulated dogs, it is probable that these animals possess a great degree of sensitivity to this poison.

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**Studies of Uranium-Poisoning. V. The Influence of Light on Uranium-Poisoning in Guinea-Pigs.**

*H. T. Karsner, Tsun Chee Shen and S. A. Wahl, J. Med. Research, 43:1, Jan.—March, 1922.*

The possibility that light might play a part in causing variations in response to uranium poisoning in guinea-pigs was suggested by the observation of group variations when experiments were inadvertently carried out in a dark room. The work here reported was done to determine if possible whether or not poisonous amounts of uranyl nitrate are influenced in their action by the presence of light. Guinea-pigs were used, and these were observed in two groups, one kept in a room photographically dark, and the other in a room receiving diffuse daylight, but no sunlight, and further lighted by a flaming arc. The uranyl nitrate was injected in varying amounts.

It was found that animals in diffuse daylight were more resistant to uranyl nitrate than were those in darkness, and that this resistance was increased by exposure to an arc light having a biologic action equivalent to that of sunlight. The use of a glass filter over the animals in some of the experiments showed that this increase in resistance was not due to the rays of short wave length, nor did it appear to be due to increased metabolism resulting from increased bodily activity. It was further found that when eosin was injected one hour before the uranyl nitrate, and at the same site, the animals in the light were less resistant to the poisoning than were those in darkness. This leads to the suggestion that the differences noted without eosin are due, not to conditions in light as compared with darkness.

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### **1d. BACTERIOLOGY AND PARASITOLOGY.**

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**The Standardization of a Base Culture Medium.**

*Henry St. Arnaud Agate and Lillah St. Arnaud Agate, J. Roy. Army M. Corps, 38:163, London, March, 1922.*

Bacteriology, in the matter of media, has become involved in a mass of detail. Human tissues and blood are much the same the world over, and when a microscopic organism gains entry, its living culture medium is practically constant. From the fact that artificial cultivation of microorganisms is possible, it must be possible to construct a single artificial culture medium in which or on which all microorganisms can grow, given the temperature of the living body and the presence or absence of oxygen. The construction of such a medium is based on the following considerations: Reaction; presence of growth substances (vitamins); the content of amino-acids; the content of sodium chlorid. The medium is built up of meat broth and dry peptone as follows: A bullock's heart is cleaned of fat and fibrous tissue and put through a mincer; the mince is mixed with twice its weight of distilled water and made slightly alkaline to litmus paper. It is heated to 80° C. for five minutes and cooled to 37° C.; then to the total volume, Liq. tyrisinae comp., in the proportion of 1%, is added.

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It is incubated at 37°C.; and the biuret reaction tried at intervals of some hours, the time required to give a positive reaction (pink) being very variable. When the reaction is positive the mass is strained through a wire gauze sieve and through glass wool, sterilized at 100° C. for thirty minutes and allowed to cool. The reaction is then generally found to be acid, and, if not, it must be made acid to litmus paper with normal HCl. After standing for twelve hours any fat is removed from the surface with coarse filter paper. It is again subjected to 100°C. for thirty minutes, cooled and decanted. The reaction is adjusted and the amino-acid content estimated by means of a comparator and indicators. The content of sodium chlorid is fixed at 0.85% of the final volume of the constructed medium. It does not affect either reaction or amino-acid content. If before any titration or adjustment is done the broth is repeatedly sterilized at 100° C., the reaction does not alter after subsequent similiar sterilization when adjustment to pH 7.5 has been made. This method has therefore been adopted. Filter paper is not used, but only wool and gauze, since filter paper is not only too slow but causes a surprising diminution in the amino-acid content. In practice, a trypsinized ox-heart broth required 2.3 c.c. normal NaOH per hundred to bring to pH 7.5; and when adjusted the amino-acid tent was 96%. A 2% dry peptone solution required 0.4 c.c. NaOH per hundred to bring to pH 7.5, and when adjusted the amino-acid was 34%. A 1% marmite solution required 0.5 c.c. normal NoOH per hundred to bring to 7.5 and when adjusted the amino-acid content was 10%. Thus it is only necessary to reckon up the amino-acid values, add enough distilled water to get a total amino-acid content of 40% and then add 0.85% NaCl to the volume to obtain the base medium. It then becomes necessary to add one or more substances to this base medium in order that the metabolic activities of various microorganisms may be observed. For instance, admixture of agar, 3%, makes a solid medium. For nearly three years this medium has been used in routine and research work. It has been used in parallel with numerous mediums of the literature, and in no instance has failed; in the majority of instances it gave a better growth in less time than the control medium. With admixtures when necessary and the presence or absence of oxygen at a temperature of 37° C, the writers claim that this is a reliable constant standardized medium whether made in successive batches or in large bulk for storage or distribution.

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**Substitution of Brom-Thymol-Blue for Litmus in Routine Laboratory Work.**

*H. R. Baker, J. Bacteriol., 7:301, March, 1922.*

This investigation was designed to find a method of preparing mediums to determine qualitatively acid or alkali production by bacteria which would be easy to prepare, and more sensitive than litmus; and one in which the reaction could be quickly determined at any time during the incubation period. A sugar-free broth was prepared of 1 lb. ground lean beef, digested for two hours with 1 liter distilled water. This was cooked, filtered and autoclaved at 18 lb. pressure for twenty minutes. After cooling, it was inoculated with *Bacterium saccharolyte*,

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incubated at 37° C. for forty-eight hours to render it sugar-free. The medium was sterilized in the Arnold for twenty minutes, 10 gm. peptone and 5 gm. NaCl added, the reaction adjusted to pH 7.0 with brom-thymol-blue, steamed again for twenty minutes, reaction readjusted and the medium filtered.

Tabulated data show that brom-thymol-blue did not cause marked inhibition on acid production by Gram negative *Bact. coli* commune or *Bact. typhosum* and inhibited the 2 Gram positive organisms only in concentrations much higher than need be used in actual acid determinations. A 1: 41,666 soluton of brom-thymol-blue gave the most desirable concentration for colorimetric comparison. This concentration could be used without inhibiting acid production. This dilution was made by adding 12c.c. of 0.2% alcoholic solution of the indicator to every liter of sugar-free broth before it was put into fermentation tubes. The advantages of this medium are: (1) As brom-thymol-blue includes the neutral point in its range of hydrogen ion concentration, the medium can be adjusted to exact neutrality before being inoculated. (2) A medium containing sufficient brom-thymol-blue to act as an indicator will not inhibit acid production. (3) Brom-thymol-blue is not reduced by microbial action. (4) The reaction of carbohydrate medium containing brom-thymol-blue can be recorded at any time during incubation. (5) Changes in color with slight changes in hydrogen ion concentration are more marked with brom-thymol-blue than with litmus. (6) Brom-thymol-blue is easier to prepare than litmus. (7) Heat does not affect brom-thymol-blue during sterilization. (8) The reaction of carbohydrate broth containing brom-thymol-blue can be read by artificial light, impossible with litmus.

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. Notes on the Gram Stain with Description of a New Method.

*Victor Burke, J. Bacteriol., 7:159, March, 1922.*

This paper gives the results of experiments comparing aqueous solutions of various domestic dye-stuffs and their value as substitutes for the anilin gentian violet solution in the Gram method. Aqueous solutions (1%) of 6 samples of methyl violet, 3 of gentian violet, and 1 of crystal violet were used and compared. Some of the dyes improved with age. As dyes gave variable and in most cases unsatisfactory results, the experiments were extended to an analysis of the factors determining the Gram reaction in the hope of modifying the staining method so that satisfactory results could be obtained with more domestic dyes. These experiments included the determination of the effect of heat, of acid and alkali added to the primary stain on the slide, of washing between the solutions, of heat on the iodin solution, of different decolorizes, and of water on decolorization. Pure cultures of *Staphylococcus aureus*, *Bacterium typhosum*, *Neisseria catarrhalis* and *N. gonorrhoeae* were used. They were grown for approximately twenty-four hours on peptic digest agar slants to which 33% hydrocele fluid had been added or in Loeffler's blood serum tubes. Mounting the films in distilled water, tap water or physiologic salt solution did not affect the straining reaction. Jensen's method and a modification of this was used.

The modified method of making a Gram stain with aqueous  
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solutions of dyes and without addition of mordants to the stock solution gives better results than any other method. Satisfactory differentiation between Gram positive and Gram negative organisms can be obtained with any of the domestic gentian violets, methyl violet and crystal violet dyes. With the better dyes certain steps in the process can be omitted or modified, but with the poorer dyes strict attention must be given to all details.

The new method is as follows: (1) Air dry thin film and apply least amount of heat necessary to kill the organisms and to fix them to the slide. (2) Flood smear with 1% aqueous solution of the dye mixed with 3 to 8 drops of 5% solution of sodium bicarbonate, allow to stand two or three minutes. (3) Flush off excess stain with iodin solution, cover with fresh iodin solution and let stand a minute or longer. (4) Wash in water and blot off all free water, but do not allow film to become dry. (5) Decolorize with acetone, or acetone (1-3 parts) and ether (1 part) until decolorizer flows from slide practically uncolored, usually less than ten seconds. (6) Let slide dry, blotting if necessary. (7) Counterstain from 5 to 10 seconds, or longer, with 2% aqueous solution of safranin O. (8) Wash off stain, blot and dry. Immerse in xylol or turpentine until clear. If the first attempt at staining a smear does not give satisfactory results, wash off the oil with xylol, wash off the xylol with acetone, and restain. Restaining gives better results. Acetone decolorizes the Gram negative organisms and the debris on the slide more rapidly, and the Gram positive organism more slowly, than does alcohol. It is cheaper, reduces time, gives better results with poorer dyes and permits use of stronger dye or mordant. The addition of water to the decolorizer retards decolorization of Gram negative organisms and increases decolorization of Gram positive organisms. Steaming the iodin solution on the slide or increasing the period of exposure does not cause the Gram negative organisms to resist decolorization. Decolorization of Gram negative organisms is delayed by drying the film after exposure to the iodin. The control of the removal of the water after the iodin and decolorization largely determine the amount of differentiation between Gram positive and Gram negative organisms. Mounting the films in sodium bicarbonate or lactic acid affects the results. The addition of the former results in greater concentration of methyl violet dye in Gram positive organisms after decolorization, and lactic acid brings about the opposite result. The failure of Gram positive organisms in old cultures and in smears from the genito-urinary tract to retain the violet dye may be due to the presence of certain acids. This suggests the possibility of enhancing the value of gentian violet in selective mediums and improving dye therapy by addition of an alkali. In attempt to reverse the Gram phenomenon, staining was found inadequate from a practical point of view for distinguishing staphylococci from gonococci in mixed infections. Experiments to determine whether the primary stain penetrates the cell wall of typhoid-like organisms showed that all of the colon-typhoid group do not differ from the gonococcus-catarrhalis group of organisms in their resistance to the penetration of methyl violet.

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**The Use of Domestic Methylene-Blue in Staining Milk By the Breed Method.**

*W. A. Wall and A. H. Robertson, J. Bacteriol., 7:307, March, 1922.*

In staining milk preparations by this method it has been found that the solutions of methylene-blue will dissolve the milk films or will wash them off. The authors undertook a series of experiments to correct these difficulties. They found that the addition of small amounts of  $\text{Na}_2\text{CO}_3$  to those solutions of methylene-blue which were reported to dissolve milk films rendered them satisfactory for use. To avoid the contamination of aqueous staining solutions, which is frequent, Loeffler's alkaline methylene-blue was tried with uniformly good results. It was later found that any solution of methylene-blue prepared in 30% alcohol was as satisfactory as Loeffler's formula, and also prevented the growth of organisms in the staining solution. These results indicate that stains prepared in alcoholic solutions are to be preferred to the aqueous solutions recommended in the Standard Methods Report; but on account of the insolubility of the zinc salt in alcohol, either the medicinal methylene-blue or some methylene-blue for bacilli which is not largely made up of zinc must be used.

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**Simplified Method for Staining Spirochaeta Pallida in Smears.**

*J. J. Puente, Rev. Asoc. méd. argentina, (Biol. Sect.) 34:1134, Buenos Aires, Nov., 1921.*

Spirochaeta pallida offers a certain resistance to staining. Hoffman's method with Giemsa's stain, although the preferred one at present, requires time-consuming technic, and the outlines are not sufficiently clear. Puente has attempted to replace it with the more practical, rapid and economical method. This consists of fixation in a bath of formal (2), acetic acid (1), and water (100), followed by an alcohol-ether fixing bath; heating, after filtration, and staining in a solution of tannic acid (5%) (3 parts), and hydrochlorate of anilin (3%) (1 part); after it has cooled a washing with hot water, and staining with boracic methylene-blue. The object of the first fixation bath is partially to dissolve the albumins, which would otherwise darken the field, as they take the stain diffusely. The filtrate obviates erroneous interpretations, due to the great quantity of yeast and moss found in tannin. This method saves time in making multiple preparations. Treponema pallidum stains blue. The differentiation must be based upon morphologic characteristics.

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**The Effect of Metals on Bacteria.**

*A. Schnabel, Klin. Wchnschr., 1: 389, Berlin, Feb. 18, 1922.*

The first observations regarding the action of heavy metals on living cells were made by the botanist Nägeli and the dentist Miller, who described this action as oligodynamic. This word is still used to characterize the phenomena produced by the action of heavy metals on cells. In reviewing the numerous articles which discuss this action a certain discrepancy in the results of the experiments is noticeable.

The experiments were performed by putting pieces of metal into a fresh, recently coagulated and inoculated nutritive medium, or by producing a certain bactericidal action in water and by putting pieces of metal in it for several days. As it is well known that heavy metals are only slightly soluble in water the explanation of this action of metal must be that an electrochemical solution of metal is produced by the development of an electrical potential, or by dissolved metallic salts. The presence of metal in water activated in this way has been demonstrated repeatedly, and such activated water behaves like a solution of metallic salts. It is, for example, inactivated by ammonium sulphate, weakened in its action by albumin bodies (formation of metallic albumins) and also shows, like solutions of metallic salts, diffusibility and capacity for concentration on evaporation. This diffusibility explains the action of metal on bacteria in coagulating nutritive medium, while in nutritive medium that is already coagulated, there is no action. The action of metal in fluid nutritive medium becomes apparent within a few hours, while the effect from dipping metal in the water does not become apparent for days or weeks. Further experiments show that, by volatilization, the metal exercises an action on the nutritive medium or water when it is separated from these substances by a layer of air or by a porous membrane.

These experiments show that the action of metal is due to a process of solution, but the question remains open as to what brings about the solution of the metals. That the atmospheric air plays a part in it is indicated by the fact that inactive metals become active after lying in the air. Electrochemical processes may also help to dissolve the metals. This is indicated by the observation that one metal strengthens or weakens another in its action. A distinction is to be made between bactericidal and growth-inhibiting properties of metals. Other experiments are concerned with the property possessed by metals and metallic salts of modifying the toxicity of bacterial albumin and bacterial toxins; for instance, tetanus and diphtheria toxins are markedly weakened by the action of copper. But unfortunately the slight effectiveness of dilute solutions and the toxicity of concentrated solutions prevent its use for internal treatment. Colloidal solutions of heavy metals also affect bacteria but there is a decided difference between the effects in vitro and in animal experiments.

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**The Digestibility of Bacteria.**

*C. E. Dukes, Brit. M. I., London, March 18, 1922, p. 430.*

Although nitrogenous substances form the basis of bacterial cells, yet bacteria are not digested by powerful proteolytic ferments, and are capable of living and multiplying in a solution which would split up those proteins of which, by chemical analysis, bacteria have been shown to be composed. That this resistant faculty is not dependent on the fact of life is demonstrated by the experience that bacteria are also not digested when killed by weak antiseptics, or at low temperature. Owing to this property, bacteria continue their existence when surrounded by the digestive juices of the intestinal canal, and also continue to thrive in a culture medium into which enzymes have been excreted by other bacteria. Experiments were undertaken to study the  
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conditions under which bacteria resist digestion, and under what conditions this protective property can be destroyed. As a result of adsorption tests, it was found that bacteria do not adsorb proteolytic ferments. From the digestion experiments it was seen that those agencies which most readily destroy the bacterial antitrypsin are all fat solvents (alcohol, acetone, ether, chloroform, and alkalis). The lipoids contained by bacteria, because of their effect on surface tension, are probably concentrated round the periphery of the bacterial cells, and form a protective covering for the organism. The protein of bacteria is protected from the action of proteolytic ferments by the lipoid envelope. The agencies which destroy this protective mechanism act by disturbing the lipoid distribution. Finally, the antibodies present in immune serum do not in any way render bacteria more digestible by trypsin, although the contrary has been claimed by other investigators.

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**On the Presence of Nucleic Acid in Bacteria.**

*Alexander J. Schaffer, Caspar Folkoff and S. Bayne-Jones, Bull. Johns Hopkins Hosp., 33:151, April, 1922.*

Bayne-Jones and his collaborators have succeeded in preparing, from massive cultures of *B. coli* grown upon a synthetic medium containing no purin or pyramidin compounds, a substance containing the amount of phosphorus required for plant nucleic acid, and also containing guanin. It is certainly a member of the group of substances called nucleic acid, but does not contain the crucial pentose group of plant nucleic acid; on the other hand it does not seem to be exactly similar to nucleic acid from animal tissues, since the method of preparation was one which, as found by its originators, W. Jones and Folkoff, does not isolate nucleic acid from animal tissues.

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**Influence of Vacuum upon Growth of Some Aërobic Spore-Bearing Bacteria.**

*L. D. Bushnell, J. Bacteriol., 7:283, March, 1922.*

Various investigators have found *Bacillus mesentericus* and *B. subtilis* in unspoiled canned goods. The reasons for this condition are: (1) Spores of certain types predominate on the product as it goes into the container. (2) Spores of certain types are more resistant to heat than spores of other types. (3) The spores of certain types are not all destroyed during the processing period and those remaining are able to grow under conditions as they exist in the container. Bushnell undertook a number of experiments to determine why *B. mesentericus* predominates in canned goods. He considered this series: (1) The influence of different amounts of air upon the growth of the organisms; (2) The influence of varying amounts of salt, acid and air upon the growth and thermal death point of the organisms; (3) The influence of lactic, tartaric and citric acids upon the thermal death point of the organisms. The amount of vacuum under which spores of these organisms were placed during the heating did not influence the thermal death point. The small amount of acid present had but slight retarding

influence upon the growth of these organisms in air, but a marked influence was observed upon the thermal death point. It may be that the beneficial influence of acid upon the keeping of canned goods is due more to the lowering of the thermal death point than to the inhibition of growth. The amount of air present in the containers had no influence whatever upon the thermal death point of the bacteria and very little upon the growth. In the case of the organic acids the same result was noticeable, only acetic acid has more effect on the thermal death point. Bushnell believes that *B. mesentericus* predominates in canned food because it is capable of growing to some extent without air, rather than because its spores are more heat resistant than some other types of aerobic bacteria.

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**A Method for the Cultivation of Anaërobes.**

*L. D. Bushnell, J. Bacteriol., 7:277, March, 1922.*

The most commonly recommended methods of cultivating anaërobes are difficult to apply, requiring complicated apparatus, and they are expensive and time consuming. For three years Bushnell has used the Sellers method for removing the oxygen by the use of metallic phosphorus. He finds it the most convenient and effective of all the methods recommended. Obligate anaërobes have been grown on plates, on slant agar and in liquid media under anaërobic conditions produced by phosphorus. One of the greatest advantages of this method is the small amount of phosphorus required to absorb the oxygen in the jar and that which leaks in. Water will absorb the phosphorus acid anhydrides. An aluminum pressure food cooker, manufactured by the Pressure Cooker Company, of Denver, Colo., was used for an anaërobic jar. The pressure gage on the top is removed and the opening plugged. Rubber cement is smeared around the edge before using. This jar will retain a vacuum of 4-5 inches of mercury for as long as two weeks in the incubator at 37° C. Water is placed in the bottom of the jar, cultures are placed on a wire rack, an evaporating dish containing the phosphorus is placed in the jar and covered with a bit of wire gauze having a small opening in the center. This prevents the burning phosphorus from spattering. When all is ready one of the stopcocks in the cover is opened and the cover is held so that it may be replaced quickly. The phosphorus is ignited by a hot needle passed through the hole in the gauze. The cover is replaced and screwed down. The pet-cock is shut off after a few seconds and leaks are watched for. The pet-cock should be left open until the positive pressure from the burning is neutralized. The capacity of the jar is about 25 plates or 80 test-tubes of 1.5 mm. diameter. Bits of phosphorus must not be allowed to remain exposed to the air.

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**Modification of an Improved Anaërobe Jar.**

*J. Howard Brown, J. Exper. Med., 35:467, April, 1922.*

The explosion of an anaërobe jar, after use for a year without accident, has led to a slight modification of the apparatus. The accident was due to the breaking of one of the copper wires which had become corroded from contact with the rubber stoppers, resulting in the pro-

duction of a spark when the electric current was turned on. The corrosion may be avoided by having the copper wires enter the coil through the bore of a glass tube, joining the nichrome wire through small holes in the side of the tube within the coil. Although the capillary rubber tubing used in insulation has no corrosive action on the copper wires, it is further suggested that wire insulated with a noncorrosive insulation such as asbestos be used. The bore of the glass tube is also packed with asbestos at either end where the wires pass into it and the joint is wrapped with insulating tape.

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**Methods for the Isolation of Filter-Passing Anaërobic Organisms from Human Nasopharyngeal Secretions.**

*Peter K. Olitsky and Frederick L. Gates, J. A. M. A., 78:1020, Apr. 8, 1922.*

In November, 1918, the authors isolated from the filtered nasopharyngeal secretions of influenza patients, and from the lung tissues of rabbits intratracheally inoculated with these secretions, an organism which they called *Bacterium pneumosintes*. As originally isolated, it was a minute bacillloid body, of regular form, with a length of about 2 to 3 times its breadth, measuring from 0.15 to 0.3 micron in its long axis. It passed Berkefeld filters, multiplied slowly only under strictly anaërobic conditions in a medium composed of human ascitic fluid and a fragment of fresh rabbit kidney, and withstood glycerolation for a period of months. It decolorized by Gram's method and stained with the usual basic dyes. Various similar methods of cultivation have been tried, some of which were successful. Rabbits immunized with the organism develop specific precipitins, agglutinins, bacteriotropins and complement-fixing bodies. The most suitable organisms which may be used as a method of enrichment of the culture medium are *Bacillus mesentericus*, *B. coli*, *B. typhosus*, and the pneumococcus Type III. Time is saved by a primary incubation to establish anaërobic conditions and insure sterility.

Suggestions are made for the bacteriologic examination of nasopharyngeal secretions in cases of respiratory disease apparently not due to ordinary aërobic bacteria. It seems not unlikely that *Bacterium pneumosintes* is only one of a number of related or unrelated, anaërobic, filter-passing organisms which may be obtained from human sources by appropriate methods.

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**. The Circulation of Bacteria in the Mouth.**

*Arthur L. Bloomfield, Bull. Johns Hopkins Hosp., 33:145, April, 1922.*

In experimenting with cultures of the harmless organism *Sarcina lutea* inoculated into various parts of the mouth cavity, it was found that the organisms were in general not transferred to other areas in the mouth cavity, except in the direction of the pharynx, so that there was a progression toward the esophagus. Organisms inoculated on the tonsil or pharynx did not move forward into the mouth nor did the drink-  
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ing of a large glass of water remove any great number. Those organisms that were removed were swallowed and not reimplanted in other parts of the mouth or throat. When thick suspensions of *Sarcina lutea* were drunk, relatively few organisms adhered to the mucous membranes; the greatest number were recovered from the tongue, with a few from the tonsils. Not wishing to use pathogenic organisms experimentally. Bloomfield studied the distribution of bacteria in the mouths and throats of a number of carriers of various organisms. Here also the same laws of progression were found to hold, the organisms spreading from the primary site of colonization only in the direction of the esophagus.

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**Diphtheria Bacillus Carriers. Results of Reëxamination of Apparently Negative Cultures.**

*B. C. Marshall and C. G. Guthrie, Bull. Johns Hopkins Hosp., 33: 110, March, 1922.*

If cultures from the throats of diphtheria carriers are examined only once, after twenty-four hours' incubation, as is often the custom in routine examinations, an error may be made because some of those which appear negative actually contain organisms. A second examination after forty-eight hours will reveal diphtheria in the lagging cultures. Marshall and Guthrie made their studies upon carriers, but a similar series has been reported by Knebel, which was obtained from persons convalescing from diphtheria. Knebel's results were almost mathematically identical with those of the authors; combining the 2 series, it is found that of 1125 cultures negative at the 24 hour examination, 107 were positive at 48 hours. This possible error, amounting to 9.5%, is called to the attention of workers interested in securing accurate statistics in regard to diphtheria and the carrier state.

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**Disinfection Studies. The Effects of Temperature and Hydrogen-Ion Concentration upon the Viability of Bact. Coli and Bact. Typhosum in Water.**

*Barnett Cohen, J. Bacteriol., 7:183, March, 1922.*

In this research Cohen has investigated the effects of variations in moderate temperature and moderate hydrogen-ion concentrations upon the death rate in water and dilute buffer solutions. These determinations have been utilized to study some of the characteristics of that phase of disinfection produced by mild factors, which for want of a better term Cohen has called sublethal. By a brief review of the literature it is shown that previous investigators have observed the effects of temperature and hydrogen-ion concentration on the death rate of bacteria. In the large mass of experimental work, the descriptive material of which is clarified by many tables and graphs, the author tested the response of bacteria to the sublethal factors (in contradistinction to disinfection as ordinarily understood) of starvation and moderate intensities of hydrogen-ion concentrations; the effect of moderate temperatures upon the rate of this response, and the analysis of the behavior in the light of the physicochemical concept of the disinfection process. The method

of study pursued was to expose *Bact. coli* and *Bact. typhosum* to a given solution and follow periodically the numbers of survivors capable of forming colonies on nutrient broth. By these methods a study was made of the viability of *Bact. coli* and *Bact. typhosum* at 0°, 10°, 20°, and 30°, in double distilled water, in tap water and in dilute buffer solutions.

From these experiments Cohen concludes that at constant temperature the mortality of bacteria in unbuffered mediums like distilled or tap water is variable and coincident with apparently insignificant pH variations. Controlling pH by means of M/500 buffer solutions stabilizes this variability. The subjecting of organisms of the colon-typhoid group to these mild lethal conditions tends to magnify the induction period prior to mortality at the maximum or logarithmic rate. Thus the early response of the organism to the disinfection process can be studied. Higher acidity and higher temperature decrease the period of induction. It appears to have a duration inversely proportional to some exponent of the temperature. It is analogous to the induction period occurring in chemical reactions. At constant pH, the relative resistance of *Bact. coli* to *Bact. typhosum* decreases with the rise of temperature from 0°:10°:20°:30° in the ratio of 67:51:18:8. At 20° C. *Bact. typhosum* possesses the greatest tolerance within a narrow zone of hydrogen-ion concentration delimited by pH 5.0 and 6.4 A slight increase in acidity beyond the zone results in conditions of maximum mortality. For *Bact. coli* the zone is wider and centered about absolute neutrality. Cohen and Clark found that the pH optimum for growth and fermentation of bacteria may be different. It is now shown that the optimum for tolerance may also be distinct. The mortality of bacteria, whether by strong disinfectants or by milder agents, follows the laws of logarithmic decline which can be expressed mathematically.

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**The Influence of the Gastric Juice on the Bacteria of the Typhoid-Coli-Dysentery Group.**

*K. Hajos, Wien. Arch. f. inn. Med., 3: 453, Jan. 20, 1922.*

The experiment was performed by the use of gastric juice: (1) obtained after (a) a test breakfast, (b) feeding of 300 c.c. of water, (c) an apparent meal (no actual food given); (2) with hyperchlorhydria; (3) with hypochlorhydria; (4) in which the pepsin was removed by heating; (5) in which the hydrochloric acid was neutralized by animal charcoal. Old bacteria of the coli-typhoid group and of dysentery were added and determined. The bacteria were later killed. Corresponding HCl solutions served as controls.

Result: The bactericidal and disinfectant power of the gastric juice depends on the quantity of free HCl alone. The total acidity supports the action of the free HCl. Normal gastric juice kills the bacteria in about fifteen minutes. Bacteria which come into the stomach and which are contained in solid substances are killed earlier than those which come into the stomach with fluids such as milk or water because the latter pass out of the stomach at an earlier period. Patients with anacidity and hypo-acidity are more susceptible to intestinal infections.

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**Some Observations on the Bacillus of Unna-Ducrey.**

*Oscar Teague and Olin Deibert, J. Med. Research, 43:61, Jan.-March, 1922.*

In a previous publication the authors outlined a simple means for the identification of the Ducrey bacillus, the diagnosis being based on the morphology and arrangement of the bacilli in a smear made after 24 hours' incubation from the pus of a suspected sore and stained by the Gram method. This work has been continued to establish the value of the method as a diagnostic procedure and to study the serologic relationships of the organism. In this latter study, however, insurmountable difficulties were encountered and no evidence was obtained. It was found that stock cultures of the Ducrey bacillus are best preserved by transplanting into clotted rabbit's blood heated at 55° C. for fifteen minutes, incubating for twenty-four hours, and then keeping the cultures in the refrigerator. Such cultures remain alive at least three weeks and sometimes four or five weeks. The bacillus showed numerous involutinal forms in clotted rabbit blood that has been heated for ten minutes at 64° C., and on blood agar plates there was a zone of hemolysis around the colonies after three or four days' incubation.

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**Bacterial Nutrition. Growth of a Hemophilic Bacillus on Media Containing only an Autoclave-Stable Substance as an Accessory Factor.**

*T. M. Rivers, Bull. Johns Hopkins Hosp., 33:149, April, 1922.*

A number of organisms have been studied to test the statements of various authors that for the growth of influenza bacilli two accessory factors are needed, one an autoclave-stable, the other an autoclave-labile substance. For his work, the first was prepared from cultures of baker's yeast, the second from blood, being actually a nearly pure hematein. It was found that *B. pertussis* grew well and could be transplanted indefinitely without either of these substances. *B. influenzae*; both hemolytic and nonhemolytic, required both of them, while another organism, *B. haemoglobinophilus canis*, required only the autoclave-stable substance. Either it does not need the autoclave-labile substance or can synthesize it or similar material. This result thus seems to throw doubt on the views of those who consider that some interaction between these two substances is necessary to enable growth in various organisms.

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**Inoculation of White Mice with Pfeiffer's Bacillus. Influenza Studies. IX.**

*N. Paul Hudson, J. Infect. Dis., 30:433, April, 1922.*

Hudson found that Pfeiffer's bacillus when injected intraperitoneally in pure culture was pathogenic for white mice irrespective of the source, and could be recovered from the heart blood by cultivation on chocolate-agar medium. Strains isolated during influenza epidemics at military camps were more pathogenic for white mice than those from other sources. The invasiveness of both Pfeiffer's bacillus (Sec. 1—Page 935)

and Streptococcus viridans seemed to have been increased by injections in mixed cultures: the bacillus by injection with pneumococcus, and the coccus by injection with Pfeiffer's bacillus. Pfeiffer's bacillus was not found to be appreciably increased in virulence by passage three or four times through white mice. Sublethal doses of Pfeiffer's bacillus conferred immunity to white mice against lethal (one-half slant) and twice lethal (one slant) doses of heterologous as well as homologous strains. This immunity lasted at least eight weeks.

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**Studies on the Biology of Lactic Acid Bacteria: A Summary of Personal Investigations.**

*Costantino Gorini, J. Bacteriol., 7:271, March, 1922.*

One of the most important characteristics of many lactic acid bacteria is their acidoproteolytic property. It is maintained that this property is possessed by natural milk of acid reaction but is not observed in milk which has been altered. The detection of this characteristic is very simple and needs no chemical manipulations. The casein-cleaving properties of these organisms are indicated by the liquefaction of the casein coagulum. Coccii of the udder and fermented milk beverages have already been described as possessing acidorennin properties. The inception of casein cleavage is dependent upon temperature, composition of the medium, quality of the milk and method of sterilization. It is important to note that sometimes apparently sound cows may harbor in their udders, for longer or shorter periods of time, bacteria which sometimes prove beneficial and at other times noxious both from the hygienic as well as from the dairying standpoint. It was found that, contrary to the general belief that exposure of forty-five minutes at 60° to 80° C. is sufficient to kill nonspore forming lactic bacteria, sometimes even a temperature of 100° C. is not lethal. Many lactic acid bacteria are capable of inducing ropiness only during the early phases of incubation. By using the lactic acid bacteria in cheese manufacture the noxious, putrefying and gas-forming organisms can be eliminated and the appropriate ripening furthered.

Silage that has undergone the lactic acid fermentation is by far the best, both for cattle feeding and for subsequent cheese making. Essential to the production of a lactic silage are: (1) the use of silos with impervious foundations; (2) a semidried condition of the fodder; (3) air exclusion from the mass obtained by the use of deep layers of silage and of strong packing whereby the temperature of the silage is kept between 35° C. and 40° C.; (4) inoculation with lactic acid bacteria to insure the dried results, especially when fodders are used which are not fit for a spontaneous lactic fermentation. Gorini's results have been recently verified by various investigators.

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**Adaptation and Selection of Lactic Acid Bacilli Growing in Toxic Media.**

*C. Richet, H. Cardot and E. Bachrach, J. de physiol., et pathol. gén., 19:466, no. 4, Paris, 1922.*

As bacteria are grown successively in various media, the descend-  
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ants may undergo more or less variation from the original bacteria. This is true even of strains derived from a single bacterium. The authors have produced variation in lactic acid bacilli and tolerance to potassium arsenate and thallium nitrate. The adaptation is specific with respect to the latter. Here selection according to individual resistance occurs, but the resistance also becomes developed and increased. This development is not gradual and continuous, but progresses by sudden advances and abrupt variations in the bacterial vitality. The resistance finally becomes stable, and the resulting strain is uniformly resistant. The principle thus explained is not invariable. It is very difficult, if not impossible, to cause the lactic acid bacilli to resist mercuric chlorid. There is great individual variation in resistance to the salt, but the bacilli tend to become sensitized to the action of the mercury and soon die. The process of sterilizing the media possibly plays a part in the result. The mechanism of the bacterial resistance and the chemical actions concerned in producing the variation must be studied still further.

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Serologic and Morphologic Characteristics of the Pneumococcus.

*A. L. Urquhart, J. Roy. Army M. Corps, 38:171, London, March, 1922.*

An analysis of organisms isolated from 77 cases of pneumococcus infections is presented. Comparison made with pneumococci isolated from cases of lobar pneumonia, with those obtained from cases of pneumococcal infection other than lobar pneumonia, and a correlation of the results with those of the Rockefeller Institute and of other workers using Rockefeller antipneumococcus serums, has made it possible to compare the results with those of Lister and American workers, whereby the following conclusions have been reached: (1) The pneumococcus presents its most typical appearance in fresh body exudates, and bile solubility, and absence of hemolytic activity are almost constant characteristics of the pneumococcus. (2) For the separation of pneumococci in sputum and pus, Dudgeon's method is convenient and satisfactory. (3) The fermentation reactions of the pneumococcus are of no value for the division of the organism into types. (4) Pneumococcal antibodies corresponding to the type of pneumococcus responsible for the infection, though not present in the early stage of the disease, are usually formed in the postcritical blood serum of cases of lobar pneumonia and in later stages of some other pneumococcal infections. (5) The pneumococci responsible for lobar pneumonia and other serious pneumococcal infections in England are similar to those found in America and South Africa. (6) Type I Pneumococcus is capable of producing any of the serious infections due more commonly to Type I and Type II infections.

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Change of Acid Agglutination Optimum as Index of Bacterial Mutation.

*Paul H. De Kruif, J. Gen. Physiol., 4:387, March 20, 1922.*

Two distinct varieties of microbe have been shown to exist in  
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cultures of the bacillus of rabbit septicemia. These have been designated as Microbes D and G. The former is the variety isolated from rabbits dead of spontaneous infection with the rabbit septicemia bacillus, while Microbe G has been proved to be a true mutant of the parent D form. The sedimenting growth of Type G in broth, compared to the evenly suspended, uniformly turbid appearance of broth cultures of Type D led the author to an examination of the acid agglutination optima of the 2 types. The method consisted in mixing carefully prepared suspensions of the organism to be tested with equal volumes of buffer mixtures of varying  $C_{H^+}$ . Two buffer series were employed. Na lactate-lactic acid and Na acetate-acetic acid. All experiments were carried out by adding 1 c. c. distilled water suspension of the microbe in question to an equal volume of each of the buffer mixtures. The tubes were carefully shaken, placed in the water bath at 43° C. and readings taken at one, two, and sixteen hours. The agglutination optimum was considered to be that zone of  $C_{H^+}$  where complete flocculation occurred; that is, where sedimentation of the microbes was so perfect as to leave a water-clear supernatant fluid. The tabulated results show a distinct difference in acid agglutination optimum for the 2 forms. The optimum for Type D lies between pH 3.5 and pH 3.0. This changes during mutation, the resulting Type G mutants having in general an optimum lying between pH 4.7 and pH 3.8. These acid agglutination optimums are in the nature of physical constants for the 2 types and would imply a fundamental difference in the chemical constitution of the organisms. Animal passage brought about a still greater instability in the presence of H ions.

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**The Mechanism of Granular Growth of Rabbit Septicemia Bacillus Type G.**

*Paul H. De Kruif, J. Gen. Physiol., 4:395, March 20, 1922.*

The author desired to test the behavior of distilled water suspensions of Microbes G and D in higher  $C_{H^+}$ . Since this range was not covered by the Na lactate-lactic acid series, recourse was made to the glycocoll-HCl series of Sörensen, which covers a range from pH 3.0 to pH 1.2. This buffer series was prepared from the Sörensen chart. The pH of these mixtures was tested colorimetrically and checked by the potentiometer. The flocculating activity of this buffer series was then compared to that of the Na lactate-lactic acid series. The technic of the experiments was identical with that described in a preceding publication: 1 c. c. of the buffer mixtures was added to equal volumes of 4 times washed distilled water suspensions of Microbes D and G, bacillus of rabbit septicemia. The mixtures were placed in the water-bath at 43° C. for sixteen hours, and readings taken. The tabulated results show that the acid agglutination optimum of Microbes D and G is not independent of the nature of the buffer mixture. Glycocol-HCl buffer mixtures cause complete flocculation at high  $C_{H^+}$  (2.7 to 2.4), at which points little or no flocculation occurs with the Na lactate-lactic acid buffer series. Beef infusion has the property of broadening the acid agglutination optimum of both Microbes D and G, baccilli of rabbit septicemia. This extension is in the direction of a lower  $C_{H^+}$ . There is no evidence that the beef

infusion has the power, per se, of agglutinating these organisms. It appears merely to increase their sensitiveness to sedimentation in the presence of H-ions.

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**Mutation of the Bacillus of Rabbit Septicemia.**

*Paul H. De Kruif, J. Exper. Med., 35:561, April 1, 1922.*

Two varieties of microbe have been shown to exist in cultures of the rabbit septicemia bacillus. These organisms have been designated as Types D and G. Type D is the microbe invariably obtained at necropsy of rabbits dying from natural infection. Type G appears after artificial culture has been carried out for some time. It was important to determine whether the two varieties coexist in cultures isolated from infected rabbits, or whether Type G arises by mutation from Microbe D. The experiments were performed with pure-line strains isolated from Type D culture by the Barber method. Type G microbes, discovered in pure culture of the rabbit septicemia bacillus, have been demonstrated to arise from the parent D form by mutation. When kept for several days without transplant at 37° C., or at room temperature, or in an ice-box, the D-G mutation takes place in broth cultures of pure-line strains of Microbe D. Filtrates from six to twenty-four hour cultures of Microbe D, and to some extent by filtrates from forty-eight hour cultures, greatly inhibit mutation. Type G colonies were subjected to the differential tests, and proved in all cases to be authentic Type G cultures and did not revert to the parent D form. An effort was made to discover, if possible, the constituents of plain broth that encourage the D-G mutation. The only difference between the beef infusion and the plain broth ordinarily used was the absence of peptone. The test indicated that simple beef infusion, or 5% rabbit serum beef infusion, is very unsuitable to the D-G change. It would seem that peptone is the constituent of plain broth which favors the process. The presence of peptone in suitable concentration greatly accelerates a reaction toward which a tendency already exists. A distinct maximum of the relative number of Type G colonies as compared to the parent Type D is observable in plain broth and in some concentrations of peptone, when these are kept at 37° C. for some days without transplant. Subsequent tests show the concentration of Type G microbes to diminish. The change in acid agglutination optimum exhibited by the mutant G forms implies a distinct change in bacterial protoplasm and would seem to be one of the most fundamental mutations so far described.

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**Hemolytic Action of a Staphylococcus Due to a Fat-Splitting Enzyme.**

*Marion L. Orcutt and Paul E. Howe, J. Exper. Med., 35:409, April 1, 1922.*

In the examination of a sample of milk 2 dilutions plated in blood agar showed different effects. The plate of a 1:100 dilution indicated a pure culture of a nonhemolytic staphylococcus, while the plate of a 1:10 dilution appeared to be a true culture of hemolytic staphylococcus. Observations indicated that some constituent of the

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medium was responsible and not the presence of both a hemolytic and a nonhemolytic organism. A study was made to determine more accurately the precise factors involved and hemolysis was shown to be associated with presence of fat in the media. Similar results were obtained with 2 other strains of staphylococci. Cultures grown in plain horse-blood bouillon or in the presence of fat-free milk are not hemolytic, while cultures grown in the presence of cream or other fats are hemolytic. Through the action of ether or chloroform, the organism itself is killed, but hemolysis of the red blood corpuscles is effected by the culture fluid. If heated, the living culture or the etherized culture fluid is not capable of hemolyzing the red blood corpuscles, but if allowed to stand with cream or other fat for several hours and then heated, the resulting fluid is capable of producing hemolysis. Therefore, the hemolysis is the result of the action of fatty acid upon the red blood cells and the fatty acid is formed from the cream or fat by an extracellular enzyme elaborated by the staphylococcus. The occurrence of hemolysis due to the action of a lipase upon fat necessitates the consideration of two factors: (a) the presence of a lipase, and (b) the elimination of its lipolytic action before concluding that hemolysis is due to another type of hemolytic agent.

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**Differentiation of Hemolytic Streptococci from Human and Bovine Sources by the Hydrolysis of Sodium Hippurate.**

*S. Henry Ayres and Phillip Ruff, J. Infect. Dis., 30:388, April, 1922.*

Hemolytic streptococci of human origin bear a close resemblance to those of bovine origin, but have been differentiated by differences in their hemolytic activity, the human type being approximately 100 times as active as the bovine, and its final hydrogen-ion concentration. Since, however, these differences in hemolysis and in acid-producing power might be considered as differences in degree rather than fundamental, other means of differentiation were needed; and, it having been observed that one of the authors' cultures of human streptococci did not hydrolyze sodium hippurate, while a culture of bovine origin split it into benzoic acid and glycocoll, further studies along this line were carried out. It was found that hippuric acid was hydrolyzed by 44 hemolytic streptococci from the udders of cows, but not by 33 hemolytic streptococci of human origin in the authors' collection. As much as 1% of hippurate were split into benzoic acid and glycocoll. Under the experimental conditions of the work, hydrolysis was not affected by the hydrogen-ion concentration of the medium. The composition of the medium did not appear to affect the hydrolysis, provided it was suitable for the growth of the streptococci. The hydrolysis of sodium hippurate seemed to separate the hemolytic beta streptococci of the bovine udder from those of human origin, but should be used at present only with these types. It is hoped that this reaction will be found to be equally valuable after large numbers of cultures have been examined.

Particular attention is called to the fact that the usefulness of the hydrolysis of sodium hippurate is discussed only in its relation to the beta hemolytic streptococci of human and bovine origin. These studies

have shown that the ability of streptococci to split sodium hippurate is not limited to the hemolytic types. Some of the alpha types from the udder of the cow do not produce the hydrolysis, while, on the other hand, the hydrolyzing property, is common in the lactic type of streptococci. The test must not be applied indiscriminately, therefore, to all groups of streptococci.

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**Streptococci in Chronic Respiratory Infections.**

*W. Ray Hodge and Cecile Cohen, J. Infect. Dis., 30:400, April, 1922.*

This study was carried out chiefly to determine the constancy or inconstancy of types of streptococci occurring in chronic nontuberculous respiratory infections. Brown's method of classification was employed. It was found that in patients with bronchial asthma the streptococcal flora in various samples of sputum from the same source is fairly constant and quite complex, from 8 to 14 types of streptococci occurring in single specimens. The streptococcal flora in various particles from the same sample of sputum is remarkably constant. The simple method of using a twenty-four hour serum broth culture of a washed particle of sputum as a basis for vaccine preparation seems as efficient as any, the streptococcal flora in such a culture being approximately parallel to that in the sputum itself. There is, in general, a close parallelism between the grouping of streptococci by biochemical (fermentation) reactions and that by serologic (agglutination) reactions. Certain members (alpha prime 2.1) of Brown's suggested alpha prime group of streptococci are of particular interest, these strains being universally agglutinated by all of the 7 antistreptococcal serums, but producing agglutinins active against their own type of strain only. Absorption experiments indicate that this organism contains a fundamental unit which occurs in each one of the more complicated streptococci used for immunization in this series. The position of the other alpha prime organisms is more definite, and it may be assumed that the members of this group possess distinctive cultural and immunological characteristics.

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**The Increase of Virulence of Acid-Fast Saprophytes by Passage through Animals.**

*Bruno Lange, Deutsch. med. Wchnschr., 48:350, Berlin, March 17, 1922.*

There was no change, even with a stay of several months, of acid-fast saprophytes in warm-blooded animals. No increased virulence could be established in any case. Probably the organisms were genuine tuberculosis bacilli if it is true that Kelle, Schlossberger and Pfannenstiehl succeeded in making acid-fast saphophytes virulent by passage through animals so that the passage cultures finally caused generalized tuberculosis. No one has succeeded in transmitting the closely related strains of human and bovine tuberculosis bacilli. The same is true of the alleged change of tuberculosis bacilli into the so-called cold-blooded tuberculosis bacilli. Especially striking is the assumption that it was possible to change the acid-fast frog bacillus Tb18

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into genuine tuberculosis bacilli after a single passage through animals. The findings in the experimental animals can be explained only by presuming the existence of a complicated infection including genuine tuberculosis bacilli.

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**The Behavior of Cultures of Chick Embryo Tissue Containing Avian Tubercle Bacilli.**

*D. T. Smith, H. S. Willis and M. R. Lewis, Am. Rev. Tuberc.*  
6:21, March, 1922.

In this study of the behavior of the embryonic chick cell toward avian tubercle bacilli, the authors call attention to the tendency of discarding the theory that the cell makes purposeful movements toward taking in a foreign body, ingesting or engulfing it. According to the more recent interpretation, the coming together of the cell and the foreign body is a purely chance occurrence and the taking in of the foreign body is a physical phenomenon. The findings in this investigation tend to demonstrate that the cell lacks sensibility. Observations on tissue cultures afforded a means by which behavior of living cells toward living tubercle bacilli should be followed under experimental conditions which were not greatly injurious to either form. Tubercle bacilli were ingested by clasmacytes, fibroblasts, white blood-cells, endothelial cells, ectodermal cells, liver cells, kidney tubule cells and cells lining the bronchioles and alveoli of the lungs. No microorganisms were observed in red blood-cells, striated muscle cells, nerve cells, or ciliated epithelial cells. The phenomena accompanying the appearance of tubercle bacilli within these cells were precisely the same as those shown by similar cells in regard to other foreign bodies. Entrance into cells was dependent upon the consistency of the cytoplasm of the cell, the composition of the foreign body and the position of the foreign body in relation to the surface of the cell. Contrary to the generally accepted idea, the cell did not make any active movements toward the bacillus, nor was any migration of bacilli toward the cell observed.

The number of microorganisms taken in by the cell and the rapidity of the process varied greatly with different types of cells. The clasmacytes were the most active; after that, the giant cell, the non-granular white blood-cell, the granular white blood-cell, and the fibroblast, in the order named. Once inside the cell, the bacilli were moved back and forth in the cytoplasm in a manner characteristic of included foreign bodies. In the course of time a small vacuole formed about the microorganisms, which was completely destroyed. The presence of tubercle bacilli within the cell or in the explant did not stimulate the formation of giant cells. The emulsion injected into the peritoneum of pigeons produced progressive disease of moderate severity.

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**A Study of Ammonia Production by a Certain Strain of Avirulent Human Tubercle Bacillus.**

*Alfred W. Bosworth, Marion G. Elkins, and Marguerite E. Blanchard, J. Infect. Dis., 30:357, April, 1922.*

A six weeks' study was made of the nitrogenous metabolism of a  
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certain avirulent culture of human tubercle bacilli, and it was found that in plain, dextrose, mannitol and glycerol broths there was a continuous production of ammonia. Over 30% of the nitrogen originally present in the medium may be converted into ammonia the greater part of which is lost through volatilization, although a portion is partly retained in the medium. This loss of ammonia is coincident with an alkaline reaction of the medium. No recession in the production of ammonia by the organisms was observed during the period covered by the experiments (six weeks); and it is concluded that the waxing and waning of ammonia described by Kendall is due to 2 factors: (1) a continuous production of ammonia by the organism; and (2) a loss of ammonia from the medium into the air by volatilization. So long as the medium remains acid both the total nitrogen and the ammonia contents of the broth show no decrease, but when it becomes alkaline a decrease in both occurs. If ammonia is utilized by the tubercle bacilli, the amount is extremely small in comparison with the amount lost by volatilization.

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**The Utilization of Dextrose by the Tubercl Bacillus.**

*Clarence J. Gamble and Margaret C. Herrick, Am. Rev. Tuberc., 6:44, March, 1, 1922.*

The authors report on series of experiments undertaken to show by definite quantitative methods whether sugars were consumed. Five strains of *B. tuberculosis*, 2 human, 2 bovine and 1 avian, were shown by a quantitative method to consume dextrose from a liquid medium. Folin's colorimetric method for blood sugar, slightly modified, has been selected as the most suitable for the estimation of sugar in broth. According to the tables given, each of the 5 strains consumed sugar to an extent from 12% to 80% of the amount originally present. Owing to differences in growth in the parallel cultures, a uniform decrease in sugar could not be secured. The amount consumed, however, runs closely parallel to the amount of growth recorded, and where this is equal or increased the disappearance of sugar is progressive. It has thus been conclusively proved that dextrose is consumed.

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**Homogenization in Examination of Sputums for Tubercl Bacilli.**

*Ernst Gjørup and S. V. Bagger, Ugeskr. f. Laeger., 84:275, Copenhagen, March 16, 1922.*

Of all methods for homogenization of tubercle bacilli in expectorations, Gjørup and Bagger have found that Depeignes' method with the modification proposed by Bagger yields the best results. Depeignes hit upon that method quite by accident; some samples of sputum having been put in the autoclave without being examined, he found that these samples gave beautifully uniform preparations, with well-colored bacilli. The method with Bagger's modification is executed as follows: the sputum is poured into a centrifuge-tube, covered with water and put in the autoclave. Then it is centrifuged, and with the precipitates smears are prepared. The centrifuge must be electric (about (Sec. 1—Page 943)

3000 rotations per minute); the duration of centrifuging must never be under ten minutes. Ziehl-Nielsen's stain is used but with a modification in the preparation of the carbolfuchsin: 2 gm. fuchsin are diluted with 20 c. c. alcohol (96%) and afterward put in the incubator for twenty-four hours at 37° C. Then 200 gm. carbolic acid solution is added. The method yields as good results as others, because the precipitate is always sufficient, in a not inspissated and not viscous fluid. Finally, all manipulations are made on sterile materials and the danger of pollution and of contamination is avoided. Depeignes originally put his preparations in the autoclave after having poured them in a Petri dish. The use of the centrifuge saves time and useless manipulations.

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**The Inhibitory Action of Certain Organic Mercury Compounds on the Growth of Human Tuberle Bacilli. Studies on the Biochemistry and Chemotherapy of Tuberculosis. XXII.**

*Lydia M. DeWitt, J. Infect. Dis., 30:363, April, 1922.*

Of the chemicals so far tested by DeWitt in studying the chemotherapy of tuberculosis, certain organic compounds of mercury have offered the most promise, and the present report is concerned with the growth inhibiting action of 10 organic mercury compounds of phenol, nitro and nitroso phenols, and saligenin or phenolcarbinol, and of other organic mercury compounds of anilin, the nitranilins, and methyl and ethyl anilins and nitranilins. It was found that the power of phenol to inhibit the growth of the human tubercle bacillus is greatly increased by the substitution of a mercury salt for one of the hydrogens, and is also increased by the substitution of one  $\text{NO}_2$  group for one hydrogen in the ring. The position of the  $\text{NO}_2$  group has much to do with the degree of increase of the inhibitory power, the ortho position being most favorable and the para position next; this is probably due to a quinoidal change in the phenol nucleus. The position of the mercury group has much influence on the degree of increase of inhibitory power, the ortho position seeming most favorable. The mercury bridge compounds, also seem to have a high inhibitory power, at least in the two compounds tested, in both of which the bridge occupies the ortho position. Saligenin, or phenol carbinol, has the same inhibitory power as phenol, but its mercury derivatives have a greatly increased efficiency varying somewhat with the percentage of mercury; although one compound with less mercury, but in which both a nitro and mercury group occupy the ortho position with respect to the hydroxy group, has a higher inhibitory power. In the anilin compounds also the substitution of a mercury group greatly increases the efficiency. The nitro group also increases the inhibitory efficiency, but not in the same order of position as in the nitro phenols, since the quinoid change does not readily take place in the anilin nucleus. However, the anilin compounds having the nitro group in the ortho position and the mercury salt in the para position seem more efficient than if the order is reversed. Methyl and ethyl groups do not materially affect the antiseptic power of the aniline compounds, although these compounds having methyl or ethyl groups plus nitro groups plus mercury groups have a very high antiseptic power, not apparently varying much either with the percentage of mercury or with the relative position of the different groups.

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**Microorganisms Concerned in the Oxidation of Sulphur in the Soil. I.**

*Selman A. Waksman, J. Bacteriol., 7:231, March, 1922.*

The true sulphur bacteria are the oxidizing bacteria which are by their physiologic and morphologic differences divided into the following groups: (1) colorless thread-forming bacteria, accumulating sulphur within their cells; (2) colorless, non-thread-forming bacteria, accumulating sulphur within their cells; (3) purple bacteria oxidizing sulphur and accumulating it within their cells; (4) bacteria oxidizing sulphur and sulphur compounds but accumulating it outside their cells; (5) bacteria oxidizing elementary sulphur and not accumulating any sulphur within or without their cells. The first three groups are found in sulphur springs, canal and mud waters, curative muds, river water and sea water; they oxidize hydrogen sulphid and sulphids but not elementary sulphur. Group 4 bacteria are found in sea water, canal water and soil and are able to oxidize sulphids, thiosulphates and elementary sulphur, forming a heavy pellicle on the surface of the medium. Bacteria of the fifth group occur in soils to which elementary sulphur has been added, particularly in soil-sulphur composts, oxidizing primarily elementary sulphur, thiosulphates to a small extent, but not hydrogen sulphid or sulphids. These bacteria grow uniformly throughout the medium, not forming any pellicle, liberating no sulphur and allowing a very intensive production of  $H_2SO_4$ , with the necessary carbon derived from the  $CO_2$  of the atmosphere. This group is morphologically related to group 4 but includes organisms very small in size and its bacteria are the strongest sulphur-oxidizing and acid-producing bacteria known.

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**The Human Intestinal Ameba, Iodamoeba Williamsi, and Its Cysts (Iodin Cysts).**

*W. H. Taliaferro and Elery R. Becker, Am. J. Hyg., 2:188, March, 1922.*

An historical review of the investigations of workers on iodine cysts show how varied is the description and nomenclature. The writers carried out a careful study of both the motile and encysted forms, with special reference to the structure of the nucleus. Practically all of the work was carried out on specimens obtained from 2 sisters, aged 3 and 5 years. These children had no history of intestinal disorder, but they showed a rather heavy infection of intestinal protozoa. The organisms were studied in the living condition and most of the material was fixed in Schaudinn's sublimate-alcohol solution, to which varying amounts of acetic acid were added. Heidenhain's iron hematoxylin, followed with eosin, or Mann's methyl-blue-eosin stain, as modified by Dobell, was then used. Other fixatives employed were Carney's acetic acid-alcohol-chloroform mixture, Fleming's chromo-acetic-osmic mixture (strong formula). Bouin's picro-formol mixture, and chromo-aceto formalin mixture. Other stains that were used were Delafield's hematoxylin and Dobell's alcoholic iron-hematin.

The size of the nucleus of the motile ameba varies, being roughly about one-fourth the diameter of the entire specimen. The nuclear

membrane is well defined and surrounds a large central karyosome, within a single layer of peripheral granules ("peripheral chromatin") and the few fine linin strands which run from the karyosome through the layer of peripheral granules to the nuclear membrane. The peripheral granules show a different staining reaction from the karyosome. The nucleus of the cysts contains the same structures as that of the motile amebas, except that the karyosome of the cysts becomes eccentrically placed, and the peripheral granules, which vary greatly in number among the different nuclei, become localized on one side of the karyosome, between it and the nuclear membrane. Comparison with the findings of previous investigators shows that with the exception of the linin strands, this description agrees with that of Dobell. The crescent-shaped mass described by Brug and Nöller, in the nuclei of the cysts, is composed of the peripheral granules. In cysts which are stained with iron hematoxylin and decolorized to too great an extent, the writers found many pictures similar to *Endolimax nana*, which may explain the findings of Kofoid, Kornhauser and Swezy. The structure of the ameba of the iodine cysts makes it impossible to identify it with *E. nana* or even to include it in the genus *Endolimax*. If the crescent-shaped mass were composed of the same type of chromatin as the karyosome the nucleus would resemble an *Endolimax* nucleus; but this is not the case, for the crescent-shaped mass is an aggregation of the same type of large granules which surround the karyosome in the motile stage. The writers believe that the name of the iodin cysts should be *Iodamoeba williamsi*, Prowazek, 1911.

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Racial Multiplicity in the Three Forms of the Malarial Parasite.

*E. Marchoux, Bull. Soc. de path. exot., 15:108, Paris, Feb. 8, 1922.*

Marchoux is of the opinion that there are in reality not three species or varieties of *Plasmodium*, but 3 distinct groups of malarial parasites, with a considerable number of varieties. In *Plasmodium falciparum* found along the West Coast of Africa the gametes are few in number and of oval form, whereas in that observed in Southern Italy and Macedonia the gametes are numerous and crescentic. There are slight variations between the type found in West Africa and Madagascar, while the type observed in Indo-China occupies an intermediary position between the African and European varieties. The parasite found in Greece, is readily distinguishable from that in Macedonia. A number of atypical and special forms have been described by Stephens, Craig, Vialatte and Marzinowsky.

*P. vivax* in France differs from that in North Africa, and neither of these are identical with those of the Cape Verde Islands and of the Amazon. The quartan parasite of North Africa is distinct from *P. malariae* of Solonica, while Cruz has described a special variety in the Amazon region. Immunity reactions also support a theory of racial multiplicity. The Senegalese are resistant to malaria in their own country but become infected in Dahomey, and those immune while resident along the coast may contract the disease when transported to the interior.

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**A Flagellate Parasite (Crithidia Oxycareni N. Sp.) of the Insect Oxycarenus Lavateroe.**

*G. Franchini, Bull. Soc. de path. exot., 15:113, Paris, Feb. 8, 1922.*

These parasites occur in the digestive tract, salivary glands and proboscis of the insect. The insects inhabit the shrub *Altea syriaca*. When present, the flagellum is very motile. There are several forms. The very long form measures 26-32 by 1.5 microns. The medium size is 17-24 by 1-2 microns. There are dividing forms, large forms without flagella and small, leishmania-like forms. The parasite may be readily cultivated on Nöller's gelose medium. Injections of the parasite were made into the peritoneal cavity of a white mouse and a few of the small forms were recovered from the blood, liver, spleen and bone marrow. The parasite was found in fecal deposits on the leaves, bark and fruit of *Altea syriaca*. Were the plant structure sufficiently delicate, and were a nutritive juice present, invasion by the parasite would be possible. A mechanism of plant infection is thus indicated.

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**A New Flagellate Parasite of the Juice of Two Apocynaceous Plants.**

*G. Franchini, Bull. Soc. de path. exot., 15:109, Paris, Feb. 8, 1922.*

The parasites were found in specimens of *Funtumia elastica* and *Thevetia nereifolia* growing in the greenhouse of the agricultural school at Florence. Smears of the sap or juice were fixed with alcohol-ether and stained with iron hematoxylin and by the Giemsa method. The protozoal parasite is long or oval and often without flagellum. When present, the latter is short. The parasites were free or enclosed in cell-like formations. The free forms were the larger. The length varied from 7-15 microns, the width from 4-10 microns. The flagellate forms occurred in funtumias only. In thevetias, the elongated forms were infrequent, most of the parasites being rounded or oval. The parasite resembles the form classed as *herpetomonas*. There is no helicoid formation, as in *euphorbias*. The enclosed forms seem to be in process of reproduction. The host plants do not appear to be injured by the parasites although the death of certain specimens has not been explained.

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**Mixed Bacteriophagi.**

*Oskar Bail and Tai Watanabe, Wien. klin. Wochenschr., 35:169, Feb. 23, 1922.*

In a previous publication it was said that a certain species of bacteriophagus did not always produce an identical effect upon microorganisms of one definite species.

A Shiga bacteriophage was found to be composed of 2 different fractional bacteriophagi, one of which produced large holes in the

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growth layer of an agar plate, while the holes produced by the other one on the same plate are small. Afterward it was found that this species contained a third fractional bacteriophagus, characterized by holes of medium size. Other bacteriophagi were also found to be composed of several different fractional bacteriophagi. The individual fractional bacteriophagi are cultivated in the pure state from the same plate which is inoculated with the diluted bacteriophagi in such a way that the individual holes produced by the different bacteriophagi are sufficiently separated on its surface. Bouillons, containing Shiga bacteria, are then inoculated separately with the products of the small and the large holes. But only the small bacteriophagus can be easily cultivated in the pure state, while the large and the medium ones always contain some small ones, because it is very difficult to decide whether the place of a large hole was not previously occupied by a small one. The original mixed bacteriophagus has a much greater clarifying effect upon the bouillon inoculated with Shiga bacteria than any of the fractional bacteriophagi cultivated in a pure state, which permit the bacteria to grow in lumps. By mixing pure cultures of the fractional bacteriophagi, the effectiveness of the original mixed bacteriophagus can be attained.

The independence of the fractional bacteriophagi can also be proven serologically. If the immunity serum of the small bacteriophagus is allowed to act upon the original bacteriophagus, hardly any effect can be detected, while the large bacteriophagus forms its large holes all over the bacteria layer of the plate, but the serum of the large bacteriophagus produces only small holes. The effectiveness of the original bacteriophagus can be increased if its culture is continued in such a way that the large bacteriophagus begins to predominate. Even when the plate method indicates the presence of bacteriophagi, they sometimes fail to clarify a bouillon culture. This always happens when the original culture did not contain large bacteriophagus, but only the small and medium ones, as these do not prevent turbidness in the buillon.

The comparison of 2 species, which apparently produced identical effects upon the Shiga bacillus and also seemed to be very closely related serologically disclosed considerable difference. The small serum of the one species, for instance, did not produce an effect upon the small bacteriophagus of the other species. It is thus evident that the nature of the mixed bacteriophaus can be established only by separating and studying each individual fractional bacteriophagus.

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**A Suggested Modification of the Wright Opsonic Technic  
Based upon the Differential White Blood Count.**

*Howard B. Cross, Bull. Johns Hopkins Hosp., 33:142, April, 1922.*

Cross points out that the value of the opsonic index as a measure of resistance to bacteria, is rendered obscure by several possibilities: (1) the test measures the phagocytic power of the leukocytes only, and not that of the fixed cells of the body, which is a relatively important factor; (2) in test-tube phagocytosis one may be merely observing the engulfment of the enfeebled portion of the infective hordes of bacteria, the active organisms escaping study; (3) the quantity of organ-

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isms taken up is determined by the number of phagocytes present, but the possibility of variations in this number is not allowed for in the Wright method. Cross proposes to correct the readings to allow for this last possibility, by making a differential count of the blood of the infected animal or patient. The number of neutrophile leukocytes actually present in 1 c.mm. of blood at the time of determining the opsonic index, is divided by the average neutrophile count of the same species, and the resultant figure is taken to multiply the Wright opsonic index, thus proportioning the index to the number of neutrophile leukocytes. This differential opsonic index, usually larger than the Wright index, except in some cases of leukopenia, seems to be a more dependable measure of phagocytic defense than the Wright opsonic index.

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### **Cellular and Humoral Immunity in the Caterpillar.**

*S. Metalnikow and H. Gaschen, Ann. de l'Inst. Pasteur, 36:233, Paris, March, 1922.*

The caterpillar group studied was *Galleria mell*. These insects can be readily immunized not only against *Bacillus typhosus* and *B. dysenteriae* and other moderately virulent bacteria, but against *Bacillus proteus*, *B. coli* and *Vibrio cholerae*. They are very sensitive to infection with cholera vibrios, produced by an injection of an emulsion of the living bacteria. Infection does not occur if the vibrios are swallowed. Two conditions may be produced. Virulent cultures cause fatal septicemia. Cultures of a mild type produce intoxication, Pfeiffer's reaction and marked bacteriolysis. Dysentery bacilli have the same effects. The rapidity of immunization depends on virulence. Cultures of a mild type produce immunity in three hours, virulent cultures in from fifteen to twenty-four hours. The blood cells react energetically to injections of living and heated cultures, the phagocytes diminishing in one or two hours. The lymphocytes and proleukocytes increase to 80-90%. The spherical cells increase and then disintegrate and represent an important factor in the production of immunity. The cellular reactions are more active after immunization; phagocytosis takes two or three hours before, and only fifteen to forty minutes after immunization. For Pfeiffer's reaction, the respective periods are three to four hours, and fifteen to thirty minutes. The immunity results from a very complicated reflex (involuntary) reaction of the cells. Positive and negative chemotaxis is followed by phagocytosis. Ferments and antibodies are then liberated by leukolysis and phagolysis, and the spherical cells react. Giant cells and capsules are formed and the hematopoietic tissues react. In higher animals, vessels and nerves share in these reactions. The latter differ specifically in duration, intensity and sensitiveness, according to the infecting bacteria (*V. cholerae*, *Bacillus anthracis* or *B. tuberculosis*). Immunity produces a greater sensitiveness to the infecting bacteria, and constitutes a protective effort against microbic invaders.

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**The Nature of Antigens.**

*Morgagni, 64:81, Milan, Feb. 25, 1922.*

All the so-called immunity reactions (or of antigen upon antibody), agglutination, precipitation, fixation of the complement, neutralization between toxin and antitoxin, are only different phases of a single phenomenon, related to colloidal differences: each of these may be produced with any antigen provided the proper colloidal condition is established.

Thus, for example, rather than speak of the lysins and toxins of the diphtheria bacillus, which no one has as yet seen, it would be better to speak of the various colloidal conditions of the partial fat antigens of the bacillus itself. In this class of phenomena, the proteids would have no rôle except that of eventual modifiers of the surroundings in which the specific fats assume the characteristic conditions of dispersion.

The specificity of a toxin would be the effect: (1) of special composition of the fatty acids involved; (2) of the special form (in the physicochemical sense) of the substances in which these are distributed or dispersed. By the dispersion of sodium oleate in fibrin and kaolin, the alcoholic fermentation of glucose was effected; in other words, a sodium salt of a fatty acid had exercised upon the molecule of the glucose the same action which until now it was believed could be produced only by yeast cells or by the fermentation to which these give rise. The confirmation of this finding of the fermentative power of sodium oleate would have a tremendous effect upon present theories in fermentology.

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**Antibody Production after Intratracheal Injection of Antigen.**

*Rigney D'Aunoy, J. Infect. Dis., 30:347, April, 1922.*

D'Aunoy studied the comparative antibody production in guinea-pigs and rabbits after injection of antigen by the intraperitoneal, intravenous, and intratracheal routes. It was found that the agglutinins produced by the intratracheal inoculation of *Bacillus typhosus* or of *Bacillus dysenteriae* appear as readily and in as large quantity as when the intravenous method is used, and in greater quantity than when the injection is made intraperitoneally. Precipitins can be demonstrated in as high titer in animals injected intratracheally with human and horse serums as when such injections are made intravenously. Lysins for human and sheep erythrocytes are produced by intratracheal injections, but the time required is longer than when intravenous injections of similar quantities of antigens are made. Bacteriolysins for *Vibrio cholera* are elaborated earlier and in larger quantities following intratracheal injections than following intraperitoneal injections. No fatal results followed attempts at producing various antibodies by intratracheal methods. The further study of suggested, especially with the use of antigens of virulent organisms this apparently safe and efficient method of antibody production is for which the ordinary laboratory animals are highly susceptible.

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Immunologic Reactions of Bence-Jones Proteins. II. Differences between Bence-Jones Proteins from Various Sources.

S. Bayne-Jones and D. Wright Wilson, *Bull. Johns Hopkins Hosp.*, 33:119, April, 1922.

The authors obtained 12 specimens of Bence-Jones protein from the urine of 5 patients who had Bence-Jones proteinuria associated with several different diseases. The specimens were compared immunologically with each other by the methods of precipitin reaction and complement fixation, and anaphylactic tests were made with these preparations in guinea-pigs. One of the proteins was crystalline and acted as a single antigen; the others contained traces of human serum proteins. Thus there was some confusion, except in tests in which the pure crystalline antigen was used, but the reactions were sufficiently clear to demonstrate that among the samples of Bence-Jones protein there were grouped a number of proteins, similar but not identical. At least 2, and perhaps 3, groups are recognizable by immunologic tests. The methods of isolation had no effect upon the reactions, nor was there any obvious correlation between the types of proteins and the diseases affecting the patients from whom they were obtained.

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Experimental Testicular Tuberculosis in the Rabbit.

Maurice I. Smith, *J. Med. Research*, 43:45, Jan-March, 1922.

For the study of the chemotherapy of tuberculosis it is desirable to have some means of producing in the experimental animal a definite tuberculous lesion, which can be frequently examined and on which the effects of treatment can be easily determined. The testicle offers a convenient site, and the rabbit because of its partial immunity to human tuberculosis is a satisfactory animal for the purpose. When 1 c.c. of an emulsion of human tubercle bacilli containing 5 mg. of moist bacilli to the cubic centimeter of physiologic salt solution was injected into the body of the testicle, the lesion developed, as a rule, in from two to three weeks. In none of the animals did the other testicle become infected, and there was thus available a convenient means of comparison. The lungs were involved in about half the cases, and miliary tubercles developed in the liver and spleen in less than one-fifth. The testicular lesion was steadily progressive, whether the infection spread to other organs or not. Smears made from caseating areas in the testicle or epididymis at the necropsy showed abundant tubercle bacilli but no other organisms.

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The Action of Killed Tubercl Bacilli.

H. Selter, *Klin. Wchnschr.*, 1:419, Berlin, Feb. 25, 1922

Koch did not succeed in bringing about true immunization of guinea-pigs either with old tuberculin or with emulsion of bacilli. Much thought he had attained this object by the use of bacilli dissolved in lactic acid; but a testing of his results by others, including Selter, (Sec. 1—Page 951)

showed absolutely negative results. Selter used Much's method of dissolving the bacilli and also used pepsin and trypsin. He also had negative results in his attempts to render guinea-pigs sensitive to tuberculin by preliminary injection of large amounts of killed tubercle bacilli. The animals treated in this way showed only slight symptoms of anaphylaxis. Killed tubercle bacilli did not cause immunity in normal animals; their effect on animals with tuberculosis is due to their tuberculin content; Much's lactic acid solutions are only a form of tuberculin.

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**The Influence of Tuberculin upon the Production of Antibodies.**

*Harold L. Thompson, J. Med. Research, 43:37, Jan. March 1922.*

Thompson studied specifically the effect of tuberculin on the formation of antibodies to foreign erythrocytes, observing at intervals antisheep erythrocyte titer of the serums of several groups of rabbits that had received intravenous injections of sheep erythrocytes. One series received injections of tuberculin followed by sheep cells, the other received the sheep cells only. Tuberculin (old), Tuberculin B. E. (Parke, Davis & Co.,) and old tuberculin made in the laboratory were used. Comparison of the antibody titer in the serum of the two groups showed that the injection of tuberculin into rabbits, before the injection of sheep erythrocytes as antigen, markedly increased the production of specific hemolysis. It has been assumed that tuberculin may contain a reagent which, in irritating endothelial phagocytes, would modify antibody production, and the experiments demonstrate that such a modification does occur, and that it increases the production of antibodies. Microscopic examination of the tissues of animals injected with tuberculin alone also confirms previous observations as to a profound modification of the endothelium of the liver and spleen leading to the formation of multinucleated phagocytic giant cells.

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**Experimental Studies on the Etiology of Typhus Fever. IV. Immunizing and Toxic Agents Found Occasionally in Filtrates of Typhus-Infected Tissues.**

*Peter K. Olitsky, J. Exper. Med., 35:469, April 1, 1922.*

In a previous article it was demonstrated that the typhus virus present in the tissues of guinea-pigs at the height of their reaction to inoculation is not filterable through tested Berkefeld filters. This paper shows that these filtrates, which are free from a living, multiplying agent, can occasionally induce in guinea-pigs not only the typical lesions of the disease, but also immunity to later infections of the active virus.

The brain and spleen obtained from guinea-pigs during the height of experimental infection were chosen as sources of typhus virus, because these organs contain the virus in greater concentration than the blood. In a small number of instances other effects than typhus are produced by the inoculation of filtrates from typhus-infected tissues. In 5 of 20 guinea-pigs, a rise in temperature occurred which lasted from one to three days. One of 9 guinea-pigs remained immune and 2

others of this series responded with a mild reaction, after a test injection with active virus. Four of 10 animals showed the characteristic lesions of the experimental disease. The possibility of the presence of subinfective quantities of the virus in filtrates producing the results can be eliminated. Furthermore, transmission of the virus from animal to animal by means of filtrates has failed. These experiments demonstrate that such filtrates can produce occasionally an early and short febrile reaction, immunity to later injections of active virus, and lesions indistinguishable from those of the typical experimental disease. From this is inferred that a specific substance may be present in the tissues of infected guinea-pigs and be occasionally obtainable in filtrates. The general indications are that this substance is not a living organism.

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**Sensitized and Living Anticholera Vaccine.**

*S. Masaki, Ann. de l'Inst. Pasteur, 36:273, Paris, March, 1922.*

Antirabic and antisheep-pox vaccines being prepared from living virus, the author has devised an anticholera vaccine based on the same principle. The vitality of the cholera vibrio is weakened by exposure to the action of anticholera serum. Cultures made from vibrios thoroughly exposed are negative. The vibrios are best sensitized at a temperature of 37° C. The greater the time during which the vibrios are in contact with the serum, the weaker the action of the living, sensitized vaccine. The latter is prepared as follows: Highly agglutinating anticholera serum (1:600) is diluted to one-fourth its volume with normal saline solution. Of the diluted serum 4 c. c. is added to a tube containing a 24 hour culture of living vibrios on gelose. The mixture may be incubated or left at laboratory temperature. The deposit of vibrios, washed 3 times in normal saline, constitutes the vaccine. Inoculated into the peritoneum or under the skin, the vaccine does not extend, but remains localized. It confers a definite immunity against 3 times the quantity of living vibrios constituting the regular lethal dose. The immunity is rapidly produced (in twelve to forty-eight hours). The greater rapidity is produced by small doses, intraperitoneal injection and greater exposure of the vibrios to the serum. Half a tube of the vaccine produced immunity for three months; two tubes immunized for five months. The vaccine is harmless.

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**Studies of Intravital Hemolysis.**

*R. Bieling and S. Isaac, Klin. Wochenschr., 1:373, Berlin, Feb. 18, 1922.*

On intravital injection of hemolytic immune serum the erythrocytes first absorbed this serum and then collect in the pulp of the spleen where the dissolution of the erythrocytes begins. The blood pigment set free is partly excreted by the kidneys causing hemoglobinuria and partly transformed into bile pigment, causing icterus. When heterologous blood corpuscles are injected they also collect in the spleen, as do blood corpuscles which have been changed by chemical toxins. But this capacity for accumulating changed corpuscles, is  
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not possessed by the spleen alone, for after extirpation of the spleen and injection of hemolytic serum, hemoglobinuria and icterus develop just the same, which leads to the conclusion that there is some other tissue present in the organism in sufficient amount to take over this function.

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**The Inhibition of Sodium Oleate Hemolysis by the Serum in Different Diseases, Particularly in Malignant Tumors.**

*Herbert Kahn and Paul Pottthoff, Klin. Wchnschr., 1:372, Berlin, Feb. 18, 1922.*

Extracts of the spleen, thymus and pancreas have a hemolytic action; this hemolysis is inhibited by serum. The degree of inhibition differs with the serums of normal and of sick individuals. Instead of extract of pancreas, the exact chemical identification of which is not possible, the author used sodium oleate, whose hemolytic action, like that of pancreatic juice, is inhibited to a much greater degree by normal serums than by the serum of cancer patients.

Further experiments with this method using serums from different diseases and from patients with malignant tumors showed that with less than 0.75 c. c. of sodium oleate solution there was inhibition: (1) in most infectious diseases with high fever; (2) in some hemolytic anemias, and (3) in malignant tumors. As the first 2 groups can generally be easily excluded clinically, if there is inhibition with less than 0.75 c. c. of sodium oleate solution, it indicates malignant tumor, and this may be used practically in the differential diagnosis of such tumors.

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**The Biochemistry of Phosphatids and Stearins. The Significance of the Relationship of Cholesterin-Lecithin of the Body Surface for the Stability of Erythrocyte Suspension and for Natural Hemolysis.**

*R. Brinckman and H. Wastl, Biochem. Ztschr., 124:25, Berlin, Nov. 21, 1921.*

In capacity for agglutination, the important factors are the plasma and charge of the erythrocytes, the surface tension between the erythrocytes and the suspension medium and the electrical constants of the substances, which the authors call the charge surface. The colloid-chemical construction of the erythrocytic surface, as carrier of the electric and active capillary properties, is also significant. The cholesterin-lecithin relationship, ("coefficient lipocitaire" of French authors) is important for the agglutination of the erythrocytes. It was shown by Kürten that the addition of a cholesterin suspension to the blood increased the rapidity of sinking of the erythrocytes and that the addition of lecithin decreased it. The covering normally absorbed at the surface of the erythrocyte is supposed to affect agglutination through its relative lipoidal construction.

The generally accepted parallelism between agglutination and sinking does not exist with a somewhat coarser agglutination, as was observed, for example, in serum inactivated by heat; the clumping may become so intense that the sinking disappears almost entirely. In micro-

determination elaborated for estimating the rapidity of sinking, the blood was aspirated by a capillary pipette from the bleeding finger and was mixed in a small dish with a very small amount of saturated sodium oxalate solution; with glass capillaries the blood was put into small test-tubes, filled up to a certain mark, well sealed with staniol, and placed in a rack in the thermostat. The tubes were 6 cm. long and 1.5 mm. broad and supplied with a marker at 0.1 cm. Regarding the dependence of the rapidity of sinking upon the slant of the tubes, an angle of 45° was found to be the most favorable. The erythrocytes in the plasma are believed to have a covering, which consists mainly of phosphatids and stearins and can be removed by washing 3 or 4 times with normal saline solution. If the specific agglutination depends upon the properties of this covering, this should disappear with washing out of the lipoid; in fact, the erythrocytes lose their specific rapidity of sinking in the salt solution because the erythrocytic surface colloids are washed out. On adding the total surface colloids to the salt solution, the erythrocytes completely recover their power of agglutination. With Bang's specific extraction, by treating the washed erythrocyte surface with freshly distilled petroleum ether for half an hour and then for twenty-four hours in absolute alcohol, the surface lipoids could be separated into a cholesterin and phosphatid extraction, and the effect of this fractioning from the surface colloid solutions upon agglutination (sinking) of the washed erythrocytes, which had lost their specific power of agglutination, could be tested. In this way it was shown that the phosphatids alone are responsible for the hemolysis of the erythrocytes, and that the phosphatids and cholesterin together restore the power of agglutination: in other words, the phosphatid fraction is the bearer of hemolyzing properties and the complex cholesterin-phosphatid is the bearer of the power of agglutination.

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**The Effect of Kaolin upon the Ultimate Components and the Power of Splitting Tributyrin of Guinea-Pig Serum.**

*O. Olsen, Biochem. Ztschr., 124:119, Berlin, Nov. 21, 1921.*

It is assumed that there are certain relations between serum hemolysis and lipolysis. The agent in the latter is supposed to be tributyrinase. In the treatment with carbonic acid, the flocculation of the complement middle portion results and after inactivation by heat, the ultimate portion, middle portion and the third component advanced by Sachs are destroyed one after the other. There is no relation between the power of splitting tributyrin, and the middle portion, and the third component of the complement. For the further elucidation of this subject, experiments were conducted with a combination of kaolin, with the shaking effect of the complement. The tests on tributyrinase were conducted by the drop method of Roma and Michaelis: the freshly prepared watery solution of tributyrin was occasionally prepared in the necessary strength with the phosphate regulator, the hydrogen-ion concentration of which was controlled by the indicator method of Michaelis. The number of drops, which were counted within definite intervals after the action of the serum upon the saturated solution of tributyrin, gave sufficiently comparative values for the amount of tributyrin splitting and also for the amount of lipase present,

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which expresses itself in a more or less rapid diminution of the large number of drops found in the saturated tributyrin solution. The hemolysis tests were conducted with a 5% suspension of sheep blood corpuscles and a high titered sheep hemolytic immune serum. The separation of the complement was accomplished with Liefmann's method of running carbonic acid through it. The complement titration, as well as the final and middle titration, was done in the usual way. The complete course of the reactions being accomplished, the reading of the results was taken after several hours' observation. These results show a certain agreement with the findings in inactivation of the complement with cobra venom. Accordingly the function of the third component is inhibited by the action of the kaolin. In the first stage of the kaolin effect, which expresses itself in a destruction of the function of the complement, a restitution was made possible by the addition of carbonic acid sediment or carbonic acid decantation, or of serum, heated for half an hour to 54° C., which showed neither the middle nor the final effect on serum treated with kaolin. In the second stage of kaolin effect, the reactivation was no longer possible by the addition of carbonic acid, but was possible if in addition to the carbonic acid sediment, serum heated for half an hour at 54° C. was also added with the serum digested with kaolin. In the third stage, even the serum heated to 54° was no longer able to hemolyze the sensitized blood corpuscles, even when combined with the serum treated with kaolin. The power of splitting tributyrin was still demonstrable in the serum treated with kaolin in the experiments conducted, at a time when the power of hemolyzing blood corpuscles with the middle product and heated serum was almost completely lost: the loss of the hemolytic power, therefore, occurred before the tributyrinase was injured. It should be noted however, that in these experiments only the tributyrin was tested, but not the power of splitting lecithin, which should be differentiated and which possibly plays an important part in the hemolysis. These experiments are a proof of the complex constitution of the complement and its final and middle part components.

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**The Relation of Hydrogen-Ion Concentration to Specific Precipitation.**

*V. R. Mason, Bull. Johns Hopkins Hosp., 33:116, March, 1922.*

In experiments in which rabbits were made immune to crystallized egg albumin the serum was obtained after the precipitin titer had reached 1:100,000 or more. This serum was incubated in tubes with the antigen, the tubes being graded in a series in which a range of H-ion concentration was produced by the addition of various amounts of sodium hydroxid and phosphoric acid. These particular reagents were chosen because they do not themselves precipitate protein and hence could not cause confusion in the readings. The results of the experiments showed that specific precipitation occurred only within the range pH 9.5 to 4.5 inclusive. Moreover, specific precipitates formed in a neutral medium were dissolved if the H-ion concentration was altered beyond the limits of this range.

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**The Agglutinogenic Action of Bacterial Fats.**

*Herman Schachenmeier, Biochem. Ztschr., 124:165, Berlin, Nov. 21, 1921.*

In the study of immunity the lipoids are acquiring an ever-increasing significance and many ascribe an antigenic character to the fats as well; the fats are believed to have an agglutinogenic action. This action was verified with the use of typhoid bacilli, staphylococci and colon bacilli, and for the production of fat emulsions, 30 agar tube slants were used. The cultures were covered with absolute alcohol, filtered after staining for twenty-four hours, dried and rubbed up fine in a mortar with glass dust, so that an extensive destruction of the bacterial bodies were achieved. The bacteria were quantitatively freed from fat with alcohol and petroleum ether; the purified extracts were concentrated and by transference into heated distilled water, emulsions were produced. The biuret, xanthoproteic, Millon's and tryptophan reactions were tested on the fat emulsions; all were negative. The residues deprived of fat were also taken up with water, shaken, and an emulsion of the albumin was made in this way. The emulsions thus produced were injected subcutaneously in amounts of 1-10 c.c. both in animals and in human beings. In the tests on man, only such individuals were chosen whose physical condition allowed an unobjectionable application of the findings. Staphylococci, colon bacilli, typhoid and paratyphoid bacilli A and B were used for agglutination. The findings were reproduced graphically, and they show that the fatty substances of bacteria are capable of producing antibodies, but the specificity of the agglutinins is relative. In some tests, agglutination was seen only in low dilutions, but in others with fairly high dilutions. A typhoid bacillus fat showed an agglutination of 1:640, but the residue poor in fat could not produce agglutinin formation.

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**The Agglutination of Red Blood-Cells in the Presence of Blood Serums.**

*Calvin B. Coulter, J. Gen. Physiol., 4:403, March 20, 1922:*

The author has previously stated the optimum for the agglutination of normal sheep cells in isotonic saccharose solution to be pH 4.75. To correct any possible error in the colorimetric measurements originally employed, electrometric determinations were made in a similar series of experiments in which graduated amounts of N/10 to N/40 HCL were added to suspensions of red blood-cells in saccharose solution and measurements made of the reaction of the supernatant fluid from which the cells were removed fifteen to thirty minutes after the addition of acid. The average pH (4.76) to the values thus found corresponded closely with the result of the colorimetric method. Cells sensitized with approximately 10 units of immune rabbit serum at pH 5.3 (the optimum for combination of the cells with the immune sensitizer) and washed with pure saccharose solution at the same reaction, were found to agglutinate most promptly at an average pH of 5.26.  
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The colorimetric method gave from a larger series the value, pH 5.3. If the cells be not washed after the addition of immune serum, which was present in a concentration of 0.5%, the optimum occurs at a slightly higher figure, pH 5.5 approximately. If a similar small volume of active normal rabbit serum be added to the cells in place of the immune serum, the optimum for the agglutination occurs at the same point, pH 5.5. The euglobulin precipitates most promptly and completely from rabbit serum diluted 1:20 with distilled water at the same reaction, pH 5.5, and it is apparent that the agglutination of the cells is intimately related to the precipitation of the serum euglobulin. The same relation was observed in the agglutination of sheep cells to which a like small amount of their own active serum had been added. The euglobulin itself was found to precipitate best from sheep serum diluted 1:20 with distilled water at approximately pH 5.5. It has been observed by another worker (Guggenheim) that if defibrinated sheep blood be washed directly with isotonic saccharose solution, the euglobulin of the serum is carried down with the cells and will serve as the mid-piece fraction of complement to persensitize the cells on the subsequent addition of sensitizer. Such a relation was noted by Coulter when sensitized sheep cells in saccharose solution were persensitized by the addition of active normal guinea-pig serum. If such serum be added in the amount of 8% of the total volume to an emulsion of sensitized cells of such concentration that 1 unit of complement is present, the optimal point for agglutination occurs at the following electrometric values: pH 6.19, 6.35, and 6.15. Values between pH 5.9 and 6.3 were obtained in 5 other experiments in which the estimation was made colorimetrically. The euglobulin was found to precipitate best from guinea-pig serum diluted 1:20 with distilled water between pH 6.2 and 6.4 (electrometric). If the cells were persensitized at pH 6.2 and washed by allowing them to settle spontaneously from pure saccharose solution of pH 6.0, the optimal point of agglutination was noted at the following reactions (electrometric): pH 5.71, 5.79, 5.76 to 6.18, 5.38 to 5.80, 5.78, and 5.69 to 5.77. This shift toward a more acid zone runs parallel with that observed in the precipitation of guinea-pig globulin which has been washed as precipitate and redissolved by bringing to pH 7.4 with NaOH. Precipitation then has its optimum between pH 5.1 and 5.7.

In explaining these results it should be noted that the addition of blood serum displaces the optimum for agglutination of red blood-cells in a salt-free medium to the reaction characteristic of flocculation of the serum euglobulin. This effect is not due merely to a mechanical entanglement of the cells by the precipitating euglobulin, since at reactions at which the latter is soluble it protects the cells from the agglutination which occurs in its absence. In the author's opinion a combination of some sort appears to take place between sheep cells and sheep, rabbit, and guinea-pig serum euglobulin, and involves a condensation of the serum protein upon the surface of the red cell. At the optimal point for agglutination of persensitized cells both mid-piece and end-piece of complement combine with the cells. Agglutination is closely related to an optimal H-ion concentration in the suspending fluid, and probably to the cell membrane, and not to a definite reaction in the anterior of the cell.

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**On Human Isohemagglutinins, with a Note on their Distribution among Some Australian Aborigines.**

*A. H. Tebbutt, M. J. Australia, 1:201, Sydney, Feb. 25, 1922.*

The method of grouping employed was to take the blood into test-tubes containing 3.8% sodium citrate solution, in which the corpuscles were washed simply by shaking and allowing it to settle in an ice-chest. The supernatant citrate solution was poured off and the corpuscles mixed with physiologic saline solution in a dilution of approximately 1 in 50 to 1 in 100. Known II and III sera were mixed with the corpuscles on a glass slide and the readings were checked under a microscope after about five minutes. Thorough mixture of serum and corpuscles was assured. Group II was smaller, and Group I larger, than Hirschfeld's figures for the English. The writer does not regard his figures as final. It would appear that Group II and Group IV, and by analogy Group III, are often hybrid. Much larger figures are necessary before the percentage frequency can be determined. It is suggested that unions of these groups with the pure recessive Group I should be studied in order to obtain this information. The corpuscles of 405 Australians have been grouped and the percentage frequency shown. This is subject to correction by larger figures. The blood corpuscles of 141 Australian aborigines have been grouped, and a high relative infrequency found for Group III as compared with Group II. The numbers examined are small compared with the numbers (500) of each race examined by L. and H. Hirschfield, but it seems very probable that the Australian aborigines will fall into the European style as regards biochemical index. Further examination of aborigines, preferably in different parts of Australia, is urged upon all interested in ethnology. With regard to blood transfusions, the writer suggests that the ideal must be to use a donor belonging to the same group as the recipient, instead of using Group I donors as a routine. The difficulty with infants is that their group may not be established until the end of the second year. The writer suggests that in the first month the infant's corpuscles be tested against the donor's serum, and that after the first month and up to two years the serum of both donor and infant be tested against the corpuscles of infant and donor respectively.

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**The Chemistry of the Wassermann Reaction. II.**

*I. Forssmann, Biochem. Ztschr., 124:185, Berlin, Nov. 21, 1921.*

During experiments on the chemistry of the Wassermann, the effect of ether upon the reaction was tested and it was found that if in a positive serum the Wassermann substance with the globulins was precipitated and the sediment solution then treated with ether, the positive reaction of the original solution disappeared: from this the conclusion was drawn that the Wassermann substance was dissolved by ether, and that it was therefore ether-soluble. As the positive reaction of the solution could be restored by the addition of ether previous to inactivation, it was assumed that in addition to the free Wassermann substance soluble in ether, there also occurs a bound, and therefore inactive, Wassermann substance in the positive serums; with an ether-evaporating (Sec. 1—Page 959)

process this is made free and capable of producing a reaction and thus the positive reaction returns. Experiments, however, explained this circumstance in another way: it was shown that when the last traces of ether were removed in *vacuo* previous to the inactivation, the ether treatment did not produce a negative reaction of the sediment solution, and that if instead of treating the sediment solution with larger quantities of ether only a small amount (for example 0.1 c.c.) was added and then the inactivation was proceeded with, the sediment solution was also made negative. The fact that ether treatment under the above mentioned circumstances could transform a positive reaction into a negative one, depends upon the circumstance that small amounts of ether remained behind in the solution after the pipetting off and that it was the inactivation of the positive solution together with these traces of ether which destroyed the positive ether reaction. The conclusions drawn from an earlier experiment are therefore refuted and the claim is made that not the attempted ether extraction, but the warming of the serum, together with the residual ether left after the pipetting and after the evaporation on standing causes the change to the negative reaction.

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**Study of the Cholesterin Content of Antigens and Its Significance in the Wassermann Reaction.**

*N. Frank, Klin. Wchnschr., 1:419, Berlin, Feb. 25, 1922.*

Using the calculated titer the author determined the amount of cholestrin contained in the antigen and found it between .013 and .016 mg. In one antigen there was considerable difference between the serologic and calculated titer; this led Frank to take up the question of whether the Wassermann reaction is dependent on the degree of dilution of an antigen or on its amount. In an extract which is a lipoid emulsion its colloidal condition must be regarded as decisive for the reaction, in analogy with the results of Lange's experiments with cerebrospinal fluid and colloidal gold. From experiments with various dilutions of the same amount of antigen and with diluted and undiluted antigen, and with different total volumes, he found that the reaction is not influenced either by a varying volume of the system nor by different dilutions or different concentrations of the antigen.

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**Isolation of the Antigen Plus Antibody Complex.**

*G. Izar and G. Caruso, Riforma med., 38:145, Naples, Feb. 13, 1922.*

With the addition of double distilled water to the antigen plus antibody complex, a precipitate is formed which, separated by centrifugation and treated with double distilled water, retains the property of fixing the complement. The precipitate possesses specific properties only when it has been obtained from fresh serum which has undergone no active rapid heating and to which no disinfectant has been added. The activity of the precipitate, measured in fixed specific complementary units, is to a certain extent proportional to the amount of added distilled water. Beyond a certain limit of added water, however, the

aspecific fixator properties of the precipitate become very pronounced. The optimum of the relation between the antigen plus antibody complex and distilled water varies according to whether it is a matter of antiox serum or of syphilitic serum, but seems to correspond (at least in the case of syphilitic serum) to the optimum for the precipitation of antibodies alone in the absence of antigens.

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**Experimental Studies of the Nasopharyngeal Secretions from Influenza Patients. VII. Serologic Reactions.**

*Peter K. Olitsky and Frederick L. Gates, J. Exper. Med., 35:553, April 1, 1922.*

During the fall and winter of 1918-1919, and the early spring of 1920, a number of specimens of blood serums were collected from patients in the active stages of epidemic influenza, or after recovery from the disease, for the purpose of studying the reactions of the serums with stains of *Bacterium pneumosintes* which had been isolated from the nasopharyngeal secretions of influenza patients and from the lung tissues of rabbits inoculated with these secretions. The results of the efforts to demonstrate specific antibodies in these serum specimens were disappointing. At the time the serums of influenza patients and of most of the affected rabbits were available, it was impossible to make use of them for lack of a suitable antigen. More recently a method has been developed by which certain pathogenic anaerobes, including *B. pneumosintes*, may be cultivated in a collodion sac dialysate of the Smith-Noguchi medium. *B. pneumosintes* grows readily in this anaerobic tissue culture dialysate, visibly clouding the clear liquid in a few hours and producing a heavy turbidity in three to five days. Injection of dialysate cultures of *B. pneumosintes* into rabbits results in the production of antibodies demonstrable by agglutination, precipitation, complement fixation, and phagocytic reactions. Four strains of *B. pneumosintes*, 3 from the first epidemic influenza wave (1918-1919) and one from the second (1920), show identical antigenic characters. The blood serum of rabbits experimentally injected with the glycerolated active material of rabbit passages contains specific agglutinins for *pneumosintes*, whereas normal rabbit serum does not.

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**An Effective Antigen for the Sachs-Georgi Reaction.**

*Gyula Daranyi, Orvosi hetil., 66:82, Budapest, Feb. 26, 1922.*

The author recommends dried powdered beef heart for the preparation of the antigen for the Sachs-Georgi reaction.

Clean beef heart muscle is ground with a meat-grinder, pressed between pieces of muslin, spread in thin layers on glass plates and dried at 50°C. The dried muscle is then ground to a flourlike powder. The raw extract is obtained by adding 10 c.c. alcohol (96%) to 2 gm. muscle powder, and extracting in a stoppered bottle for a day at 37°C. after shaking for about half an hour, the mixture is allowed to stand at room temperature for a day, and is filtered through filter paper. Alcohol (96%) 3.5 c.c., and solution of cholesterol (1:1000 in 96% alcohol) (Sec. 1—Page 961)

3.1 c.c. are added to 1 c.c. of the raw extract. This raw extract must be diluted about  $2\frac{1}{2}$  times the usual dilution of raw extract obtained from fresh heart muscle, as the powder loses about 60% in weight (water loss). The finished antigen is used according to the instructions of Sachs-Georgi. The result is read with a magnifying glass after twenty-four hours in the thermostat at  $37^{\circ}\text{C}$ . but without shaking.

The advantages of this antigen are: (1) The results are more uniform and definite because the alcohol has a concentrating effect and there is an easier and more complete extraction of the lipoids. (2) It is unnecessary to filter with addition of alcohol and cholesterin. (3) It is possible to read the results with the naked eye or with a magnifying glass and it is unnecessary to use the agglutinoscope. (4) There are no nonspecific reactions as with tuberculosis or carcinoma. (5) The dry powder keeps indefinitely and a large quantity may be prepared at one time.

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**Action of Autoserotherapy on the Albumins and Lipoids of Cancerous Serum.**

*Loeper, Debray and Tonnet, Progrès méd., 49:109, Paris, March 11, 1922.*

The passage into the blood of cancer patients of albumins and lipoids coming from the tumor explains probably some of the general manifestations of cancer, such as anemia and cachexia. It is also probable that these substances cause in the blood a hemoclastic shock and arouse defense processes. The authors have sought to increase the latter by injecting into patients their own serum. The results of this method so far seem inconclusive. In this paper are reported the changes which it may cause in the quantities of albumins, lipoids and amino-acids contained in the serum. Four patients with carcinoma of the stomach were given an injection of 10 c.c. serum every alternate day, the quantities of these substances being analyzed before the first and after the sixth injections. A comparison of the findings shows that there was little change in the amounts of total albumins. The globulins decreased rather markedly in 3 cases. In 2 the proportion of amino-acids became almost twice as great. The cholesterin content remained about the same, but the other lipoids appreciably diminished. It is interesting to note that radiotherapy gives almost opposite results.

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**The Condition of the Serum Protein after Injection of Serum.**

*Wilhelm Berger, Schweiz. med. Wchnschr., 52:225, Basel, March 2, 1922.*

The complete course of reaction of the qualitative and quantitative changes of the protein content of the blood serum after injection of foreign albumins can be best studied only after micromethods are found which allow the determination of proteins from quantities of blood of about 1.5 c.c. This will allow a sufficiently frequent examination. The author used the method of Nägeli and Rohrer. The serum from 1.5 c.c. blood is used and the refraction (R) and viscosity (N) are determined and the per cent. relation between the albumin and globulin is determined from the R N pairs according to Rohrer's tables. -The

forms of foreign albumins used in rabbits were horse serum, beef serum crystallized albumin and a suspension of sheep's red blood-cells. The reinjection effect was the same qualitatively but stronger than the first injection; intraperitoneal injection proved stronger than intravenous. The total protein content of the normal serum of a rabbit which has not been treated is 5-7% and the average globulin content was 20-40%. The variations in the globulin in normal serums is of no importance in these experiments.

The total protein content of the serum after injection of albumin shows at first a latency of one to four days, then an increase of the protein content which lasts for twenty or thirty days with increasing and decreasing variations. A slight increase of the content often remains after the injections and a second increase is quite frequent. The increase is often preceded by short diminution which is demonstrable only by daily examination. The globulin content after injection shows at first a latency lasting from a few hours to three days, then a short initial diminution, and then an increase which lasts from twenty to thirty days which has a rapid ascent, a short period of maximum height and a rapid fall. The increase in the globulin is considerable and may reach double or triple the normal content. The albumin content shows at first a period of latency which corresponds to the globulin, then a stage of diminution which may reach to even one-half the normal and may last as long as the globulin increase; the albumin increase comes very late. The cause of these changes is probably the effect of the injected albumin on certain cells, as yet unknown, which regulate the production and use of the serum protein. The serum globulin is the first to be increased and the most marked and is the least differentiated from the body albumins. The fact that the curve of the total proteins, having 2 crests, runs a different course from the curves of the globulin and albumin shows that the globulin and albumin are produced independently and that they do not originate from the same source.

Greater cognizance of the variability of the serums in the experiments must be taken in view of the fact that globulin and albumin are different in their biologic effects. The fact, recently discovered, that the reaction of albumin administered parenterally lasts weeks and even months, is something of great importance in protein-body therapy.

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**Ultramicroscopic Appearances of the Serum during Anaphylaxis and Similar Conditions.**

*W. Kopaczewski and M. Bem, J. de physiol, et de pathol. gén., 19:542, no. 2, Paris, 1922.*

Ultramicroscopic studies were made of serums subjected to the action of certain substances in the form of suspensions, sols and gels. These consisted of silicate, electrargol, gelose and eel serum. Fresh guinea-pig serum, mixed with an equal volume of the colloidal preparation, was left for an hour at 37°C., then centrifugated at 3000 revolutions for fifteen minutes, after which 4.5 c.c. of the clear, supernatant serum was injected into the jugular vein of a guinea-pig. Serum taken from the animal was then examined with the ultramicroscope and the image photographed. Light was derived from a Leitz arc-lamp, the cooled rays being condensed. Zeiss' apparatus was used, with a vertical

chamber. The Zeiss apochromatic objective No. 3, enlargement 83 diameters, and compensating ocular No. 2 were arranged in a dry system. Lumière plates, of one-half second exposure, were employed. The enlargements were made to 2500 diameters. Liquids examined were filtered and protected from dust, and every other precaution was taken. The molecular masses in the serum of animals receiving injections of gels or colloidal suspensions, at first separate and showing brownian movement, assemble into inert groups. This molecular agglomeration is quite different from the granular structure of heated serum, or the filamentous structure of agitated serum. It is also characteristic of anaphylaxis produced by the serum affected by the gel or suspension injected. In cases where anaphylactic shock is avoided by diminution of the surface tension or increase in viscosity, the molecular agglomeration does not occur. The image present in shock thus resembles that of the serum acted upon by the injected gel or colloidal suspension. Plates of great value are shown.

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**The Effect of Mineral Waters upon Anaphylaxis.**

*F. Arloing and P. Vauthey, J. de physiol. et de pathol. gén., 19:546, no. 4, Paris, 1922.*

The effects upon anaphylaxis manifested by water from 2 of the more important Vichy springs, Grande-Grille and Hôpital, were studied. The results were compared with those produced by a 5:1000 solution of sodium bicarbonate, the approximate proportions in the mineral waters mentioned. Daily injections of 2, 3, and 4 c.c. were made in guinea-pigs. The sensitizing injection of 0.1 c.c. normal horse serum was given intraperitoneally. The injection precipitating the anaphylactic shock (0.25 c.c. of the same serum) was made in the subarachnoid spaces after trepanning. It was found that the anaphylactic shock may be prevented or rendered less active by daily injections of the water from both mineral springs and a 5:1000 solution of sodium bicarbonate. Injections of 2 c.c. do not affect the shock, whose prevention or check requires 3-4 c.c. Duration is also important, at least 20 days' treatment with the injections being necessary. Sodium bicarbonate 5:1000 ameliorates, but does not abolish, the shock; water from the Vichy springs of Hôpital and Grande-Grille both ameliorates and checks it. The mineral waters were injected twenty-four hours after being taken from the springs. The results of the tests are discussed.

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**Studies in Specific Hypersensitiveness. I. The Diagnostic Cutaneous Reaction in Allergy. Comparison of the Intradermal Method (Cooke) and the Scratch Method (Schloss).**

*Aaron Brown, J. Immunol., 7:97, March, 1922.*

Since Blackley's first recorded experimental observation of cutaneous sensitiveness in allergy, many others have recorded similar results. At present, 2 methods are in vogue for the skin test in allergic conditions, namely the cutaneous or scratch method of Schloss and the intradermal or injection method of Cooke. Two forms of test proteins

are in use, the dry powdered preparations made according to the methods described by Wodehouse and the fluid preparations used by Cooke and made according to the methods described by Coca.

In this report are given the results of comparative skin tests carried out on the same individuals by the 2 methods, and with the dry extracts and the fluid preparations. In a series of 78 comparative tests the superiority of the intradermal method over the scratch method is demonstrated on the following grounds: In every case known to be clinically sensitive to a protein, the intradermal test with that protein resulted positively. The scratch test with the corresponding dry preparations resulted positively in only half the cases tested. The scratch test with the fluid preparations resulted negatively in 18% of the cases tested. Even with the more convenient and more active fluid preparations over 50% more time is required for the development of a positive reaction by the scratch technic than by the injection method. It takes less time to apply the latter. With an adequate supply of sterile syringes 20 intradermal tests can be made in five minutes, whereas it takes about thirty minutes by the scratch method. The intradermal method is not so painful as the scratch method and the resulting markings of the skin do not persist so long after the former method. Considerable convenience attaches to the use of the fluid extracts, as the same preparation is used for diagnosis and for treatment. With ordinary precautions in the preparation and use of the extracts, there is no danger of infection.

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**Studies in Specific Hypersensitiveness. II. A Comparison of Various Pollen Extracts with Reference to the Question of Their Therapeutic Value in Hay-Fever.**

*Albert Vander Veer, jr., J. Immunol., 7:113, March, 1922.*

Vander Veer undertook the study of the relative strengths of various commercial extracts used in the treatment of hay-fever because there is no recognized standard method of preparation of such extracts. Four commercial preparations were compared with corresponding extracts obtained from the Department of Applied Immunology of the New York Hospital which were made according to the method described by Coca. These extracts were designated by the name of the "Cornell preparations" and labelled E, while the commercial products were referred to as A, B, C, and D. Preliminary tests showed that only the very sensitive cases gave ophthalmic reaction to A, B, C, and D, so that only 18 cases could be compared. The strengths of the commercial products were given but not the methods of determining pollen units, nitrogen and dilution. The nitrogen in E was determined by the Kjeldahl method, and this showed the weakness of the commercial products as compared with E. The point is stressed that to obtain the full measure stronger extracts should be used which would require greater caution in their use as the concentrated extracts are more apt to cause constitutional reactions. The necessity for adequate dosage is illustrated by the case of a man who had received too weak a dose (a commercial preparation) for hay-fever, both early and late. The early hay-fever was almost entirely relieved but the late attack was unaffected. A test of his hypersensitiveness showed a positive eye reaction to timothy pollen extract E containing 0.005 mg. nitrogen to 1 c.c., but no reaction (Sec. 1—Page 965)

to ragweed pollen extract E of less than 0.1 mg. nitrogen in 1 c.c., the ratio of sensitiveness being therefore 20:1. He was given commercial extract A for the early fever and ragweed extract E (largest dose 0.16 mg.) for the late hay-fever. Since the commercial preparation contained only 0.005 mg. nitrogen, the E extract represented 30 times the former. The results were excellent, both early and late attacks being controlled. Patients vary markedly in their degree of hypersensitiveness as demonstrated in this case and also in the size of the dose necessary to relieve their symptoms. However, the use of larger and more potent doses leads to greater risk of producing constitutional, (even dangerous) reactions.

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**Studies in Hypersensitiveness. III. On Constitutional Reactions: The Dangers of the Diagnostic Cutaneous Test and Therapeutic Injection of Allergens.**

*Robert A. Cooke, J. Immunol., 7:119, March, 1922.*

By a constitutional or general reaction Cooke understands the group symptoms occurring in allergic individuals after the absorption of an allergen and its transportation by the blood and lymph into the systemic circulation. He bases his observations on the experience of ten years in the diagnosis and treatment of some 4000 allergic cases, but the data for this paper are derived from a statistical study of 578 consecutive cases in 1920. The intradermal test was used exclusively and a definite diagnosis of allergy was based upon a marked cutaneous reaction. The symptoms observed were those of the various clinical allergies and in an individual case they were usually those from which the patient suffered, with certain manifestations in tissues not reached by the allergen under ordinary exposure. The usual symptoms were coryza, asthma, urticaria, erythema, pruritus, edema and cough. The infrequent symptoms (these being observed rarely and in varying degrees) were glandular enlargement, headache, fever and chilliness, nausea, diarrhea, acute abdominal pain, dysmenorrhea, syncope and cardiac collapse.

The constitutional reaction occurs in 2 forms, the immediate and the delayed. Allergens may cause immediate constitutional reactions by whatever path they may be introduced: that is, after test, after injection or on ingestion. Several illustrations of constitutional reaction are given when the cutaneous test is immediately positive. These intradermal test reactions agree with the clinical histories or can be clinically substantiated in 95% of the cases reacting to the pollens and animal epithelium. Clinical reactions when the cutaneous test is negative are explained on the assumption of a complete absence of skin allergy with a hypersensitiveness limited to the respiratory mucous membrane. As immediate reactions Cooke considers those occurring within one hour, after which the reactions are considered as delayed. These also occur when the test is either positive or negative. The following factors are responsible for constitutional reactions: the mode of introduction of the allergen, the reactivity of the individual, activity of the allergens, concentration and dosage of the extracts, cumulative effects (with the same and different allergens) and allergens causing specific reactions.

A list is given of allergens found to cause constitutional reactions,  
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and it is suggested that a thorough knowledge of the treatment of the reactions should be had by every one attempting this type of study. With the onset of the symptoms, a tourniquet should be tightly applied about the arm above the site to be tested in order to prevent the transportation of more allergen to hypersensitive tissue through the systemic circulation. Adrenalin (1:1000), 1 c.c. for adults, 0.4 to 0.6 c.c. for children, should be given at once subcutaneously, or if the reaction is severe, intravenously. If the symptoms increase the dose should be repeated in two to five minutes.

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**Studies in Specific Hypersensitiveness. IV. New Etiologic Factors in Bronchial Asthma.**

*Robert A. Cooke, J. Immunol., 7:147, March, 1922.*

For cases of bronchial asthma not easily diagnosed by testing with extracts of substances that cause asthma, an explanation was sought along 2 lines: (1) that it was due to bacterial proteins acting as allergens, and (2) that the paroxysm of asthma was a reflex effect. Many investigators support the theory of a bacterial origin, but Cooke attempted to prove the possible allergic nature of the bacterial reactions and failed. He maintains that the conception of a bacterial asthma has been based solely on analogy, and that the analogy is not upheld by proof. It is advised that such cases should be classed as undiagnosed even though resort be had to vaccinotherapy with apparently good results. In his experience there were cases which proved that the supposedly reflexly acting mechanical excitants particularly selected by Walker, namely hay dust and house dust, are genuinely specific factors and they operate in the specifically hypersensitive individual just as do pollens, animal dander and the other well-known allergens that demonstrate their clinical effect after absorption by inhalation. The group of substances absorbed by inhalation play a much more important part as specific causative factors of asthma than is generally considered by other investigators.

All of Cooke's work is based on positive findings. He applied Coca's method of preparing dust extracts, which yielded valuable information by permitting a study of the occupational or domiciliary environment of an asthmatic and established a positive diagnosis in certain cases that could not be evaluated by any other means. This extract has shown the presence of a substance in most house dust that is in itself an important factor, although its nature and source are as yet unknown. By dialysis a considerable quantity of nitrogenous substance appeared in the dialysate, but the dialysate did not contain the reacting substance. When heated to 212° F. for thirty minutes there was a diminution in the activity of the extract, but under these conditions no precipitate formed. When heated to boiling in an open vessel so that the  $\text{CO}_2$  of the extracting fluid was driven off, some precipitation took place and the extract lost all power of reactivity in a short time. The dust of hay is not to be considered solely as a simple mechanical irritant but may act as a specific allergen.

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**Studies in Specific Hypersensitiveness. V. The Preparation of Fluid Extracts and Solutions for Use in the Diagnosis and Treatment of the Allergies with Notes on the Collection of Pollens.**

*Arthur F. Coca, J. Immunol., 7:163, March, 1922.*

Pollen extracts are often quite unstable in their activity both as diagnostic agents and as therapeutic material. To obviate this disadvantage Coca undertook the preparation of fluid extracts. It was necessary to provide a sterile preparation of not too low concentration which would remain stable for at least six months. After some experimentation, the following composition of the extracting fluid was adopted. NaCL, 0.5%, NaHCO<sub>3</sub> in such concentration that 10 c.c. of the final fluid equaled about 3 c.c. of N/10 alkali, and carbolic acid, in final concentration of 0.4%. The use of heat was avoided, as was also excessive shaking. Whenever an original extract was diluted, a portion of stock extracting fluid passed through a sterile Berkefeld and the sterilized fluid was added to the original extract. This alkaline extracting fluid was used for all dry materials (such as cereals, the danders, the nuts, and the pollens), for certain vegetables that contain little juice (such as sweet potato, fresh beans and peas) and for the meats. A "preserving fluid" was used in the case of vegetables and fruits containing considerable juice. This preserving fluid contained the same constituents as the "extracting fluid" in higher concentration, together with 2.5% NaCl, 1.25% NaHCO<sub>3</sub> and 2% carbolic acid. Extraction of dry material was carried out at room temperature for forty-eight hours (sometimes 3 days). The addition of toluol to dry materials prevented the occurrence of bacterial growth. Oil which interferes with extraction was removed with ether, which does not denature proteins. The number of changes of ether depended upon the different percentages of oily substances. Before mixture with the extracting fluid the ether was driven off. In most of the extracts and preserved juices a precipitate formed upon standing, and it is suggested that this be removed by the use of a Sharples centrifuge if the precipitate is not too voluminous. Smaller quantities of extract may be filtered through paper, preliminary to the final sterilization through Berkefeld or similar filters. In voluminous precipitates a partial separation can usually be effected with a fine mesh towel laid over a sieve. A shallow layer of toluol covering the fluid during sedimentation is advisable. The filtered extract stock was stored in 16-ounce bottles. For clinical purposes extracts were distributed in vaccine bottles or homeopathic vials, which were capped with "no-air" stoppers. The nitrogen content of all the preparations was determined by the Kjeldahl method and generally adjusted by dilution to 0.5 mgm. or less per cubic centimeter. While some general principles applied to all of the members of the several groups of materials, the method employed for each group was modified to meet certain peculiarities. Coca gives in detail the preparation of the extracts for 7 members of the dry material group, many of the moist material, miscellaneous preparations and egg, among others.

In collecting pollen care must be taken to exclude all other materials and all moisture must be eliminated from the collected pollen before it is stored. For the collection of grasses, the heads are cut off with scissors and spread in not too thick layer, upon strips of glazed paper. Be-

fore the heads are spread on paper they are shaken through a sieve to exclude extraneous matter. A warm, dry, well lighted room, protected from dust is used. In twenty-four hours, pollen drops from the heads. The heads are transferred to a fresh piece of paper and more pollen drops out. This treatment for forty-eight hours also insures complete drying, after which the pollen, heads and flowers are sifted several times, the final sifting being through a 200-mesh copper wire screen. In New York City the timothy grass pollen should be collected between June 20 and July 6, the late afternoon or evening being the most favorable time for collection. In the collection of ragweed pollen, it must be shaken off as it ripens naturally in the field. Since all the pollen does not ripen at the same time, it is profitable to begin the collection as soon as the anthers open.

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**Studies in Specific Hypersensitivity. VI. Dermatitis Venenata.**

*W. C. Spain, J. Immunol. 7:179, March, 1922.*

This investigation was designed to determine the susceptibility to "poison ivy" of adults and children. An extract was made by mixing 95% ethyl alcohol or chloroform with fresh leaves to Toxicodendron radicans. After several days a clear extract is obtained by paper filtration. Typical vesicular lesions of dermatitis were produced by the application of this extract to the skin. In these experiments the typical vesicular lesion of dermatitis venenata could not be produced by intradermal injection of an active alcoholic extract. The lesion thus produced was not different from that caused by the intradermal injection of the solvent. By means of the "patch test" differences were demonstrated in the susceptibility of different individuals to poison ivy, and in the incubation period of the lesion. This test was carried out as follows: In the center of a piece of adhesive tape, 5 by 5 cm., a piece of white blotting paper 0.5 by 0.5 cm., saturated in an alcoholic extract of Toxicodendron radicans leaves was placed on the gummed surface. Tape was then applied to the flexor surface of the forearm. The patch was removed after 3 days and the area washed free from tape and all traces of the active principle. Observations were made several times a week. A reaction was considered positive when a typical vesicular lesion of poison ivy was reproduced beneath the patch. No positive results were obtained in testing the susceptibility of 18 infants between 5 weeks and 18 months of age. For purposes of comparison Spain takes 65% as representing approximately the average susceptibility of individuals over 8 years of age with the patch test.

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**Studies in Specific Hypersensitivity. VII. The Age Incidence of Serum Disease and of Dermatitis Venenata as Compared with That of Natural Allergies.**

*Arthur F. Coca, J. Immunol. 7:193, March, 1922.*

In previous studies on specific hypersensitivity it has been shown that serum disease presents the almost constant characteristic of an incus (Sec. 1—Page 969)

bation period, and that dermatitis venenata differs from the other allergies in which the skin is involved in the constant and characteristic nature of the lesion. Serum disease differs strikingly from most of the other forms of human hypersensitiveness in its high percentage incidence. Other workers found that the percentage of individuals affected with the symptoms of the "natural" allergies increases considerably in each generation, at least in the early successive life periods. The percentages in the second and third life periods are respectively about  $2\frac{1}{2}$  and 4 times as great as in the first life period. With these facts at hand Coca made a statistical study of this question, the results of his experiments showing the following differences in the age incidence of the "natural" allergies, serum disease and dermatitis venenata: (a) The age incidence of the "natural" allergies increases rapidly in the early age periods but probably does not greatly exceed 10% in any period. (b) The age incidence of dermatitis increases greatly from childhood to adult life, reaching a high percentage, probably about 90%. (c) The age incidence of serum disease apparently does not change during life.

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**Studies in Specific Hypersensitiveness. VIII. On the Relative Susceptibility of the American Indian Race and the White Race to the Allergies and to Serum Disease.**

*Arthur F. Coca, Olin Deibert and Edward F. Menger, J. Immunol. 7:201, March, 1922.*

A questionnaire concerning the occurrence of the allergies among American Indians was sent to physicians and a superintendent of an Indian school. All of these men had had extensive experience with the Indian race, and their replies were based on observations of about 40,000 full-blooded Indians. In only a few instances had the physicians seen cases of asthma and other anaphylactic manifestations among the full-blooded American Indian. But, there was abundant evidence that such conditions are prevalent among the white race and breeds.

The authors then undertook an experimental study of allergies produced in 26 volunteer full-blood American Indians. A table shows that the incidence of the condition among those injected was 46%; the average duration of the symptoms was 2 days and the average elevation of temperature was  $0.38^{\circ}\text{F}$ . This same study was carried out on 52 Caucasians under similar conditions. In this series the incidence of serum disease was 92.4%. This incidence of serum disease is supported by Cole and other observers. The authors' work indicates that the Caucasians are more susceptible to allergies and serum disease. This similarity in the relative susceptibility of the 2 races to the allergies and serum disease suggests a similarity in the underlying mechanism of both of the conditions which need not amount to a complete identity.

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**Studies in Specific Hypersensitiveness. IX. On the Phenomenon of Hyposensitization (the Clinically Lessened Sensitiveness of Allergy).**

*Robert A. Cooke, J. Immunol. 7:219, March, 1922*

The experience of Cooke and of other investigators has been that  
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complete specific insensitiveness is not attainable in allergy. Coca ascribes this failure to a difference in nature of the relative insensitiveness as compared to desensitization in allergic conditions. The difference between these 2 effects is qualitative, and allergic hypersensitiveness of human beings is not due to the influence of precipitin—it is not anaphylaxis. Coca and Kosakai have shown that if human hypersensitivity is dependent upon the presence of precipitin, then the successive injection of identical or nearly identical quantities of the exciting agent should not cause repeated exhibition of symptoms. A multiple of the partially desensitizing dose is always required to cause symptoms upon a subsequent injection. Conversely, if symptoms, even in slight degree, recur upon such repeated injections, then precipitin can have no part in the production of the symptoms. By applying this test to the work of Alexander and Mackenzie, Cooke concludes that the serum sensitivity which they were attempting to modify was not anaphylactic in nature and that the reduced sensitiveness which they established was therefore not a partial desensitization. The phenomenon of "local exhaustion" of the allergic reaction described by Mackenzie and Baldwin is found (in disagreement with these authors) to be nonspecific. Cooke carried out experiments on himself to test the exhaustion or fatigue of the general power of reactivity on the part of the tissues to irritation. These experiments show that there is no true desensitization in allergy; that after a site has been made nearly insensitive to one concentration of the material, a vigorous reaction can be produced with a stronger concentration of the same material; that the local insensitiveness produced by the repeated injections is not specific. Cooke proposes to distinguish the lessened sensitiveness induced in allergy from the state of desensitization in anaphylaxis by designating the former condition as a state of hyposensitization.

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**Studies on the Physiologic Action of Some Protein Derivatives. IV. The Toxicity of Vaughan's Crude Soluble Poison.**

*Frank P. Underhill and Axel M. Hjort, J. Pharmacol. & Exper. Therap., 19:145, March, 1922.*

Alkaline hydrolysis of casein in absolute alcohol produced a substance having a toxic effect which proved lethal when injected intraperitoneally into guinea-pigs in doses ranging from 100-300 mg. There was a considerable variation in the toxicity of the different preparations of Vaughan's crude soluble poison. The fatal outcome following the injection of the poison occurred in two ways: (1) primary, due to respiratory failure within two hours following its administration; and (2) secondary, occurring in two to thirty-six hours as the result of a progressive asthenia. The preparations having the greater acidity proved to be the most toxic. The acid content of the poison was not alone responsible for its toxic action. The greater part of the acidity of Vaughan's crude soluble poison was uncombined hydrochloric acid. The degree of acidity of the poison depended upon the excess of acid added in the process of neutralization of the alkaline alcohol extract, and the extent of heating while evaporating to dryness. The decrease in toxicity of the poison subsequent to incubation in faintly alkaline solution was not due to a loss in its nitrogen content. Hydrochloric acid when injected intraperitoneally into guinea-pigs proved fatal in doses of 5 mg. or more,

the acuteness of the death depending upon its quantity and concentration. Acid alcohol extracts from Witte's peptone and pure deuterocaseose substances which, when evaporated to dryness in acid alcohol solution, are very toxic, and closely resemble Vaughan's crude soluble poison both in action and degree of potency. Vaughan's crude soluble poison differs from Witte's peptone and proteose in that its toxicity is not so greatly modified by evaporation in acid alcohol solution as in the case of the latter two.

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**Studies on the Physiologic Action of Some Protein Derivatives. V. The Relation of Blood Concentration to Peptone Shock.**

*Frank P. Underhill and Michael Ringer, J. Pharmacol. & Exper. Therap., 19:164, March, 1922.*

When Witte's peptone was injected into dogs in doses of 0.3-0.5 gm. per kilo in a volume of 0.9% sodium chlorid solution approximating 50 c.c., a marked fall of pressure resulted in all instances, the pressure rarely if ever returning to the initial level. The minimal point is generally maintained for several minutes, followed by a slow rise to a level approximating 80 mm. Hg, where it may remain; or else there is a secondary fall of pressure culminating in death. In other experiments the blood is indefinitely delayed. On the other hand, if the pressure returns toward the normal level, the clotting is little delayed. Dosage and rate of injection play a rôle in the development of an increased concentration of the blood. Where 0.3 gm. per kilo was injected, the rise in concentration was not so great nor so rapid as when 0.5 gm. per kilo was introduced in the same period of time, namely ten seconds. When the same dosage of peptone was injected at varying rates, the more rapid injection induced a quicker development of the concentration, although with the slower injection the ultimate degree of concentration may be greater than with the more rapid introduction of peptone. On the other hand, even with the same dosage and same rate of injection, there may be a variable response with respect to blood concentration in spite of the pressure effects being almost identical. It is quite evident, therefore, that there is an individual variation among experimental animals relative to resistance to the peptone injection. That low blood pressure in itself is not the responsible factor in blood concentration was well seen in an example of the influence of amyl nitrite upon the blood pressure. In spite of a fall of pressure, due to a general vasodilatation and hence to a decreased blood flow and probable interference with the internal respiration of the capillaries, there was no change in the concentration of the blood. It seems quite probable that the fall of pressure initially induced by Witte's peptone is not responsible for the concentration of the blood observed under the experimental conditions. The fact that a rapid injection of a dose of Witte's peptone produces a rapid effect upon blood concentration, whereas the same dose introduced in a greater interval of time produces the same degree of concentration but not so rapidly, the pressure in the two instances being practically identical, argues for the hypothesis that the quantity of peptone in the circulation at a given period is the effective agency in modifying the development of blood concentration.

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**Studies on the Physiologic Action of Some Protein Derivatives. VI. The Influence upon Blood Concentration of Vaughan's Crude Soluble Poison.**

*Frank P. Underhill and Michael Ringer, J. Pharmacol. & Exper. Therap., 19:179, March, 1922.*

The introduction into the circulation of the dog of Vaughan's crude soluble poison, in doses of 0.2-0.5 gm. per kilo, with its acid content neutralized or unneutralized, caused the production of a significant increase in the concentration of the blood. The features of this response resembled in every respect those evoked by Witte's peptone or purified proteoses. It should be stated, however, that the acid product was more toxic before than after it had been neutralized, an observation corroborating the conclusions of Vaughan and Pryer and those of Underhill and his collaborators.

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**An Experimental Study on the Effects of Protein Injections upon Infections.**

*Isidor Kross, J. Med. Research, 43:29, Jan.-March, 1922.*

From experimental work carried out on white rats, guinea-pigs and rabbits, infected in several different ways, Kross concludes that the protein treatment did not increase the resistance of the animals to mouse typhoid, general peritoneal sepsis or pneumonia, and did not enable them to overcome infection any better than did the untreated animals. On the contrary, the vitality of the animals was apparently reduced as evidenced by their more rapid destruction. The treatment consisted of the injection of 1 c.c. of 1% solution of nucleic acid given by the subcutaneous, intraperitoneal or intracardiac method.

The danger of death from anaphylactic shock must be considered, a number of deaths having occurred shortly after intravenous injections of bacterial substances. The negative results in these series and the recognized clinical dangers of the procedure indicate the need for caution in the therapeutic use of intravenous protein injection in infections.

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**Studies on the Nature of the Action of Nonspecific Protein in Disease Processes. III. Nonspecific Proteins and Soluble Toxin (Diphtheria-Tetanus).**

*David Murray Cowie and Roy Mark Greenthal, J. Med. Research, 43:21, Jan.-March, 1922.*

This series of experiments was designed to determine whether the protective action of normal horse serum, which had been previously shown to protect guinea-pigs against fatal doses of diphtheria toxin, is due to the protein or to antitoxin which may be present in horses not injected with diphtheria toxin. The horse serum was, therefore, separated into its albumin and globulin portions and the protective action of each was observed as well as that of other nonspecific proteins, and in addition the protective action of normal horse serum against tetanus toxin was determined.

The results lead to the conclusion that nonspecific proteins when  
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injected subcutaneously into guinea-pigs do not in themselves protect against a fatal dose of diphtheria toxin. Egg-white, milk, guinea-pig serum, and rabbit serum were found to have no protective value. One cubic centimeter of horse serum, however, will protect against several fatal doses of diphtheria toxin; but the protective action lies, the authors believe, not in the protein of the horse serum but in its antitoxin content. This was shown by the fact that the horse serum protein when precipitated by alcohol loses nearly all of its protective power, and that nearly all of the diphtheria antitoxin in 1 c.c., containing 1500 units, is destroyed by alcohol. The alcohol precipitated globulin of 1 c.c. diphtheria antitoxin will protect against only a single fatal dose of diphtheria toxin. The globulin fraction of normal horse serum has more protecting power than the albumin fraction. The most conclusive evidence that horse serum contains an antitoxin for soluble toxin lies, however, in the fact that no other protein protected against diphtheria toxin. These results are in accord with clinical observations that tend to show that the foreign protein injections in disease are of value in assisting the combat against bacterial invaders, and not in the destruction of toxins produced by them. They further indicate that foreign protein injections should be given early in acute diseases before a large amount of toxin is produced; late in the disease foreign protein injections do no good, they may do harm.

It was also found that 1 c.c. of normal horse serum when injected subcutaneously into a guinea-pig will protect against a fatal dose of tetanus toxin.

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#### **Phenol and Cresol as Preservatives in Biologic Products.**

*Peter Masucci, J. Infect. Dis., 30:379, April, 1922.*

In Masucci's study of preservatives, experiments were made to determine: (1) the effect of cresol and ether-cresol with time on serums in relation to the amount of precipitate formed; (2) the influence of ether in the ether-cresol mixture as to germicidal value and hemolytic power of cresol; and (3) the mechanism of the ether-cresol action on serums. The action of phenol and ether-phenol on serums was also studied in a similar manner. The following points were brought out: (1) cresol or ether-cresol changes the color of serum or plasma from a light yellow to a greenish yellow; (2) there is no marked difference in the amount of precipitate formed on standing between serums treated with straight cresol or ether-cresol; (3) the precipitate formed in normal serum is most finely divided fibrin; (4) cresol hastens the formation of fibrin in plasma; (5) cresol lowers the surface tension of serum much more markedly than phenol; (6) ether-cresol does not burn serum on account of a surface tension phenomenon; (7) cresol produces hemolysis rapidly with destruction of the hemoglobin while phenol produces only slight hemolysis with no effect on the hemoglobin under the conditions of the experiment; (8) ether does not alter the course of hemolysis in itself or as ether-cresol or ether-phenol (9) the lowering of surface tension in itself does not produce hemolysis, but substances which lower the surface tension are absorbed by the erythrocytes to a greater degree.

From this experimental data Masucci concludes that ether-cresol has no advantages as a preservative of serum over straight ether, in the total precipitate formed on standing or in germicidal value.

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**Action of Snake Venom on the Blood Composition.**

*B. A. Houssay, M. J. Otero, J. Nigrete and P. Mazzocco, Rev. Asoc. médica argentina (Biol. Sect.), 34: 299, Buenos Aires, Nov., 1921.*

Snake venom produces marked changes in the blood, especially if the venom is a coagulant, in which case a violent reaction takes place, in the form of an initial protein shock, with marked hypotension, leukopenia, temporary increase in coagulability, followed by absolute incoagulability. Most of the experiments were performed on dogs, solutions of venom—generally from *Lachesis alternatus*—were injected intravenously or subcutaneously. There was an initial fall in arterial pressure, and a decrease in the number of leukocytes, followed in from thirty minutes to an hour by an increase. The leukocytosis was predominantly polynuclear. The number of red cells did not vary during the initial leukopenia, except for slight fluctuations. The injection checked the sedimentation of erythrocytes, especially when coagulant venoms were administered as they defibrinated the blood to a marked degree and prevented precipitation. The plasma of the fresh blood was centrifuged; it was more or less red in color. This may have been due to the destruction of some red cells and the escape of their contained hemoglobin. There was a decrease in the amount of hemoglobin.

There was a precipitation of fibrinogen, so that the arterial blood became defibrinated and did not coagulate at 60° C. The total protein was diminished following the injection of coagulant venoms, or there was an increase of the globulin fraction and a diminution of the albumin fraction.

Glycemia was increased immediately following injection, reaching its maximum in about thirty or sixty minutes, and decreasing in seven or eight hours.

There was a marked and constant increase in nitrogenous protein, probably due to disintegration of the protein during the initial shock. The amount of urea, creatin and creatinin varied very little, but the total creatinin was increased. There was a slight increase in chlorid. The results for catalase, and for the alkaline reserve, were uncertain.

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**Spontaneous Decrease of the Surface Tension of Serum. I.**

*P. Lecomte du Nouy, J. Exper. Med., 35:575, April 1, 1922.*

The purpose of this paper is to report a study of this phenomenon, which has been overlooked so far, on account of lack of proper apparatus for measuring surface tension. Over 3000 measurements of the surface tension were made with the tensionmeter. From this study the author concludes that generally, after ten minutes, the surface tension reaches a value which is practically constant. At least, the decrease is very much slower. After stirring, a rise occurs and a similar phenomenon takes place; but stability is not obtained so rapidly, requiring about twenty-five minutes. By stirring again, the same thing happens repeatedly, the slope of the curve being less marked each time, the rise in surface tension being slightly below each previous value, and the phenomenon undergoing a sort of damping. An equation was established which expressed the experimental facts with an accuracy of

about 0.2%,  $t$  representing the time,  $\gamma$  the surface tension at the time,  $\gamma_0$  the surface tension at the beginning of the experiment, and  $K$  a constant. It applies to the whole phenomenon, before and after stirring. It has only one characteristic constant,  $\gamma = \gamma_0 e^{-Kt}$ . This formula, by simply changing  $t$  to  $c$  (concentration), expresses satisfactorily in general the phenomenon of adsorption in the surface layer; that is, the decrease in surface tension in function of the concentration. Prolonged heat, at 55° C., and time seem to inhibit this phenomenon. When precipitation occurs in the serum, the bottom of the liquid, which contains the precipitate, has the highest surface tension. When stirred, the surface tension rises a little every time. The upper part, clear, with lower surface tension, shows the reverse phenomenon; after every stirring, the surface tension becomes a little lower.

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**Comparative Researches on Viscosity and Ultrafiltration Velocity of Serum.**

*Alexander Ellinger and S. M. Neuschloss, Biochem. Ztschr., 127: 241, Berlin, Feb. 29, 1922.*

The capacity of the dissolved albuminoids of blood and tissue fluids for combining water is of great importance in the exchange of fluid between the blood and tissues, as well as in the secretion of urine. The influence was observed and recorded quantitatively in the frog perfusion experiment and in the ultrafilter. It was found that definite pharmacologically active substances of known and unknown constitution increase or diminish the water combining capacity of serum albumin in concentrations that approximate to those employed for their pharmacologic effects in man and animals. It was endeavored to determine how the colloidal state is influenced with such agents, by means of viscosity determinations with Ostwald's viscosimeter and by a comparison of these results with those obtained in the ultrafiltration experiment. Comparative experiments were also carried out with serums in different dilutions, with mixtures of serum and Ringer solution of various hydrogen-ion concentration, also on the influence of salts and of caffeine. It was shown that viscosity and ultrafiltration velocity may be utilized for judging alteration of the colloidal state if the control experiments with serum, without addition, give the same values before and after ultrafiltration. Should they show considerable deviations, this would point to considerable absorption in the membrane and to altered permeability.

With increasing dilution of inactivated horse serum with Ringer solution free from carbonate, viscosity diminishes and ultrafiltration velocity increases, each in a special way. The same relations are observed with changing hydrogen-ion concentration and under the influence of neutral salts. The sequence in which the anions promote intumescence, arranged in the order of increasing viscosity, represents an inversion of Hofmeister's series in the case of the concentrations employed (OSN, I, Br, Cl, acetate, sulphate, citrate). In the case of the cations investigated (Na, K, Mg, Ca) discordance in the relations is observed under the influence of Mg and Ca, which must be referred to alterations in the permeability of the filter membrane. The anions increase viscosity in the order citrate > sulphate > acetate > Cl > Br

> I > CNS. Caffein, in different concentrations, (experimental limits were 1:128,000 to 1:1000) acts in an opposite direction on the viscosity of serum to which it is added. The maximum and minimum of the curves, which represent the viscosity as a function of the caffeine concentration, are displaced in their ordinate and abscissa values in accordance with the hydrogen-ion content of the serum. Diminishing viscosity is attended, as a rule, by increasing ultrafiltration velocity. Exceptions are explained by adsorption of caffeine on the filter, which leads to alteration of concentration in the layers passing the filter, and possibly also to alterations in the permeability of the filter.

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**Chemical Blood Analysis. III. The Significance of the Ultrafiltration Method.**

*M. Richter-Quittner, Biochem. Ztschr., 124: 106, Berlin, Nov. 21, 1921.*

Proceeding from the basic principle that a proper elimination of albumin is the self-understood prerequisite of every well conducted blood analysis, Bechhold's ultrafiltration method was used for these purposes, because it can separate the colloid quantitatively from the dispersion mediums. It was important to hasten the rapidity of the ultrafiltration: in the blood this can be done with the addition of sugar, urea, or potassium salt. The field of application for ultrafiltration can be extended in blood analysis to all those methods in which the albumin must be removed. Its advantage is the saving of time and chemicals. The technic is as follows: 5 c.c. blood is diluted to 100 c.c. with a 1% potassium chlorid solution and subjected to ultrafiltration with the apparatus of Zsigmondy-Haen for three hours; it is then washed with 1% potassium chlorid solution and the nitrogen is determined in the concentrated filtrate according to the method of Kjeldahl, Pregl, or Nessler. The same process is followed in the ultrafiltration for colorimetric determination of uric acid and of chlorin. The appended tables show a complete agreement with the usual methods, especially with the ash method of Korányi; the Korányi method is better here because it consumes less time. In the determination of sodium the ultrafiltration method provides a marked simplification and in some cases a gain of several days. In the determination of potassium it was shown that a considerable part of the potassium present in the blood is bound to the albumin. As the calcium in the blood occurs in 3 forms, that is, in combination with albumin, as a nondissociated calcium salt and as calcium ions, a great significance attaches to the ultrafiltration method, the calcium ions being extraordinarily constant under physiologic conditions. In the sugar determinations by ultrafiltration, it was shown that in most of the cases the sugar value of the ultrafiltrate is smaller than that of the original total blood or plasma; for these purposes, therefore, ultrafiltration cannot be recommended. The method of ultrafiltration is also recommended because it is technically much more easily done than the method of albumin elimination and because it allows the determination of the free ions and of the cations bound to the albumin besides the albumin elimination, without the addition of chemicals. With the ultrafiltration method it is also possible to separate the inorganic and organic combinations of phosphorus of the blood; in the same way a colori-

metric bilirubin test can be done in ultrafiltrated serum without difficulty.

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**Separate Analyses of the Corpuscles and the Plasma.**

*Hsien Wu, J. Biol. Chem., 51:21, March, 1922.*

Author's method for the preparation of protein-free filtrates of the corpuscles and the plasma suitable for all the determinations included in the system of blood analysis of Folin and Wu, is as follows: The oxalated blood is centrifuged in graduated tubes until the volume of the corpuscles remains constant. The length of time required for this has been determined previously. After noting the volume of the whole blood and that of the corpuscles, carefully pipette off the plasma without disturbing the corpuscle layer. This is best done by means of a pipette connected at the upper end with soft rubber tubing. Measure a convenient volume of the plasma, dilute with 8 volumes of water, and then add .5 volume each of 10% sodium tungstate solution and two-thirds N sulfuric acid. Stopper and flask and shake. Remove the plasma that remains above the corpuscle layer as completely as possible. Insert a blood pipette into the corpuscle layer and take out a convenient volume. Lake it with 5 volumes of water and after thorough rinsing of the pipette with the corpuscle solution add 2 volumes each of the tungstate solution and the sulphuric acid. Stopper the flask and shake. The amount of plasma which cannot be removed from above the corpuscle layer is less than 0.1 c.c. and if it is desired to economize the material the whole corpuscle layer may be used for analysis without appreciable error. It is then simply washed into an Erlenmeyer flask with 5 volumes of water followed by the required amounts of tungstate and sulphuric acid. The precipitated corpuscles and plasma may be filtered immediately. The precipitated plasma should be poured on the filter, slowly at first to allow the wetting of the filter paper before any filtrate has passed through. If for any reason the precipitation is incomplete and the filtrate is turbid, the analysis can be saved by adding a few drops of normal sulphuric acid to the precipitate mixture. The plasma and corpuscle filtrates, like the filtrate of the whole blood, are perfectly clear, only faintly acid, and suitable for the determination of all constituents included in the system of blood analysis.

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**Serum and Plasma in the Ultramicroscope.**

*Ernst Salen, Biochem. Ztschr., 124: 248, Berlin, Nov. 21, 1921.*

Small particles noticed during ultramicroscopic examination were considered by Neumann to be fat and lipoids respectively, because they were extracted with ether. The amount of these small particles is variable and with a fasting stomach the serum is supposed to contain none at all. As the investigations are contradictory in this respect, experiments were conducted according to the technic used by Bechhold in the study of hemolysis. The blood specimens were taken with paraffined cannulas, coagulated at 37° C., and as soon as the serum was sufficiently separated it was immediately examined. The optical outfit consisted of a Zeiss cardioid condenser. Eighty-three specimens of

serum (taken after fasting) were examined including those of various diseases, some from syphilitics and some from healthy persons. All contained ultramicroscopically visible submicrons, which varied greatly in amount and size in the different specimens. It was also shown that human, rabbit and guinea-pig plasma contain more or less abundant submicrons independent of the intake of fat-containing food. These maintain their active motility, aggregate and do not sediment. After the administration of fat-containing food, larger and fairly refractory small particles appear, not so distinctly circumscribed as the constant particles, and with moderately lively motion. The claims of Neumann, in so far as they relate to the effect of fat-containing diet upon the optical structure of the serum, are accordingly confirmed. The less refractory and less prominent particles, occurring in the serum independent of food meals and of administration of fat, were overlooked by him. By extraction with ether, Neumann caused the submicrons appearing in the serum after fat-containing meals to disappear, thus showing that the submicrons which are not derived from fat persist in the serum. As the globulins are precipitated by dilution with distilled water and on the addition of neutral salt are redissolved, it was thought that the chemical structure of the submicrons might be determined in this way: in fact, it was shown that the formerly described submicrons constantly appearing in the serum must be considered as globulins.

Whether any conclusions can be drawn from the presence of the submicrons in the serum and from their amount and structure respectively, can be answered in this way: that to a certain extent a true picture of the complement function of the serum can be seen in the occurrence and the structure of the serum submicrons for which the fact that the complement function is particularly connected with the globulins would also speak. The ultramicroscopic picture seems, in addition to other physicochemical methods to be valuable for giving information regarding the amount and physical condition of substances present, both of which are very important in certain tests.

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**Clinical Method for the Estimation of Chlorids in Blood.**

*Herman Friend, J. Biol. Chem., 51: 115, March, 1922.*

Briefly, the author's method consists of the precipitation of the protein of the plasma by a neutral precipitant. The protein is made up to volume, filtered, and titrated directly against a standard silver nitrate solution. A chart is then consulted, avoiding all calculations.

The following reagents are used: Aluminum cream, 0.02 normal silver nitrate, and 5% solution potassium chromate. The aluminum cream is best prepared by adding to a liter of saturated aluminum alum (C. P. not necessary) concentrated  $\text{NH}_4\text{OH}$  until complete precipitation; boiling till weakly alkaline to litmus; letting stand to settle; washing by decantation till supernatant fluid is neutral to phenolphthalein; adjusting to volume of 800 c.c., placing in well-corked bottle. The procedure takes about twenty-four hours and the cream is full of chlorids. The silver nitrate reagent is made by accurately measuring from a burette 20 c.c. of 0.10 normal solution into a 100 c.c. volumetric flask and adding distilled water up to the mark. If kept in a dark bottle, this solution does not deteriorate upon short standing.

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Technic: The blood must be taken on a fasting stomach. The plasma must be separated immediately to obtain correct results. Pipette 1 c.c. of clear plasma (slight hemolysis does not interfere) into a 25 c.c. volumetric flask containing about 10 c.c. water. Add from a graduate 3 c.c. of aluminum cream and make up to volume with water. Shake well, stand ten minutes. Filter through 5 cm. dry filter paper; 22 c.c. of filtrate should be obtained. Pipette 20 c.c. of this filtrate into a 50 c.c. beaker or Erlenmeyer flask. Add 5 drops of the 5% potassium chromate. Titrate until the yellow color is changed to a first tint of dirty brown. Note number of cubic centimeters used. Consult chart for reading.

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The Distribution of Chlorin in the Blood Corpuscles and Plasma and Serum Respectively.

Augustin Muresanu, *Biochem. Ztschr.*, 124:114, Berlin, Nov. 21, 1921.

Chlorin and sodium constitute about 70% of the mineral constituents of the blood and it was assumed that the chlorin is distributed equally to the blood corpuscles and the plasma. According to Falta's theory the blood corpuscles are free of chlorin, but this is denied by others and therefore the experiments were taken up anew. The blood was taken from the vein, made noncoagulable with sodium citrate, centrifugalized and the determinations were made partly in sodium citrate plasma and partly in serum derived from centrifuging. The volume of the blood corpuscles was determined with the hematocrit. The chlorids were estimated by Korányi's method. Tests on 7 persons with healthy kidneys showed that the blood corpuscles were free of chlorin in every case. Tests undertaken in cases of renal insufficiency frequently showed considerable amounts of chlorin in the blood corpuscles of the circulating blood. It is possible that with the introduction of carbonic acid into the full blood—at least it appears so in vitro—the blood corpuscles become swollen, the plasma becomes more concentrated and the chlorin ions penetrate the blood corpuscles. This process may even be reversible. The permeability of the blood corpuscles was altered by the carbonic acid and injured and made permeable for chlorin ions. But in opposition to this theory are the facts: (1) that normal individuals have blood corpuscles free of chlorin both in the arterial and venous blood; (2) that the water content of the corpuscles of the venous blood does not differ materially from that of arterial blood; (3) that the corpuscles do not become swollen in venous congestion and that the chlorin values of the plasma and serum coincide, although the carbonic acid tension relation is not alike in both.

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A New Method for the Determination of Calcium and Thrombin in Serum.

Fred West, *J. A. M. A.*, 78:1041, April 8, 1922.

It is the purpose here to advance a method of determination of available calcium in fresh serum, and at the same time to express in terms of calcium the amount of thrombin present. Calcium determina-  
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tion is accurate, simple and rapid, involving no calculations and using only the plasma centrifuged from the citrated blood taken for the Wassermann work, and calcium controls. Thrombin depends on two factors, available calcium and prothrombin. If, then, a thrombin result is low when the calcium is normal, it follows that prothrombin is deficient. If both are normal and still the coagulation time is slow and the clot weak, fibrinogen must have been deficient. In a series of normal cases it was found that the average age-normal figure is from 9 to 10 mg. % for calcium and about 20 mg. % for calcium and thrombin. Subtracting the calcium, a figure of from 10 to 11 for thrombin is obtained. Very little variation from these figures is found in the normal cases thus far worked out. The amount of serum required is 1 c.c. Blood is taken as for the Wasserman test. The test involves no calculations; the technic is very simple, requiring no special apparatus, and calling for no chemical procedures. The time required for a serum calcium determination, with titrated plasma on hand, is approximately one hour.

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#### The Fibrin Percentage in Blood and Plasma.

*H. Gram, Acta med. Scandinav., 56:107, no. 2, Stockholm, 1922.*

The author's method for determining fibrin, as recently published (*J. Biol. Chem.*)—the plasma being obtained by centrifuging about 4.5 c.c. venous blood with 0.5 c.c. 3% citrate—has been applied to the study of a number of conditions which may be grouped as follows: normal individuals of both sexes, diseases without special variations in the fibrin content, blood diseases, infectious diseases, other diseases. The protocols were tabulated for leukocyte, red cell and platelet counts, coagulation time, hemoglobin, etc. The average fibrin content of the plasma of normal men is 0.27%, the limits being 0.20% and 0.36%. In women, the average is 0.29%, the limits 0.21% and 0.38%. The average fibrin content of whole blood in men is 0.14%, the limits 0.11% and 0.19%. In women, the blood average is 0.17%, with limits of 0.12% and 0.21%. A small variation occurs in the same individual, but it is not daily nor related to meals. Only normal variations occur in compensated heart disease, afebrile asthma or emphysema without bronchitis, gastric diseases excepting cancer, neuroses and noninfectious nervous diseases. The percentage in plasma is nearly normal in afebrile, simple anemia and polycythemia. In whole blood, fibrin is increased in anemia and low in polycythemia. In leukemia, pseudoleukemia and myeloid leukemia, the plasma percentage may be slightly increased. It is increased in hemophilia and scurvy with stomatitis, but normal in genuine purpura. The plasma percentage is low in pernicious anemia and degeneration of the liver. The liver probably influences fibrin production. Hemorrhagic diathesis does not seem due to deficient fibrin. The plasma percentage is considerably increased in croupous and bronchopneumonia, rheumatic fever, pleurisy, erysipelas, suppurations, gonorrhea, scarlet fever, angina and bronchitis. A slighter increase is present in measles, typhoid fever, influenza, tuberculosis, syphilis and malaria. The percentage falls as fever declines. Complication with a disease increasing the percentage is followed by immediate increase. The plasma percentage is also frequently increased in uncompensated heart disease, nephritis and malignant tumor. The heart

increase is due to infection present in the lung. In nephritis, infection may be associated with intoxication, the latter being more important. The increase in cancer is partly due to infection, but also occurs in tumor obstructing the gall-ducts. An ulcerated tumor with hepatic metastases may exist with normal or lowered plasma percentage of fibrin. Increase may be produced by intramuscular injection of sterile milk. The increase present in pregnancy is probably due to irritation of the liver. No variation was observed in eclampsia. Slight hepatitis is probably the cause of the increase occurring in intoxications and infections. Diminished fibrin in the plasma is a bad sign. The color of the plasma was examined by Meulengracht's method. In normal men it lies between 1 and 4, in women between 1 and 3. There is no relation between increased fibrin and degree of bilirubinemia. Extensive destruction of the hepatic parenchyma may not increase the color of the plasma. The increased fibrin present in infections is not prevented by static icterus. The increase occurring in intoxication and infection is usually accompanied by leukocytosis. Polyarthritis is an exception to this rule, while the leukocytosis present in polycythemia has no parallel increase in fibrin. The return to normal in toxic and infectious states is followed by a rapid decline in the leukocyte count, while the fibrin fall to normal requires weeks. Leukocytosis and fibrin increase appear to be independent. The fibrin percentage seems to indicate a surer, more sensitive and more durable reaction against certain infections than does the leukocyte count. Sedimentation of the blood-corpuscles depends principally upon the fibrinogen content of the plasma and percentage of cell-volume. The globulin in human blood has also a slight influence. A buffy coat is formed when the sedimentation is increased or the coagulation period prolonged.

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### The Coagulation of Blood.

*Albert Funck, Biochem. Ztschr., 124: 148, Berlin, Nov. 21, 1921.*

The application of the results and the use of physicochemical and colloid-chemical working methods seem to point to the solution of the problem of coagulation without the aid of a ferment. The nature of coagulation is supposed to consist of a reciprocal precipitation of opposing colloids. Coagulation is due to the process of transition of coagulable albuminous bodies from the alkaline hydrosol condition (fibrinogen) to the condition of gel (fibrin). The fibrinogen to be tested was prepared by Hammarsten's method; the solutions of fibrinogen which were used in the fresh state and coagulated with thrombin in twenty-five to thirty-five minutes coagulated neither spontaneously nor with a calcium salt alone. The thrombin solution was prepared according to Schmidt's method. The direction of migration was determined by Michaelis' apparatus. As the electric migration occurs only outside of the flocculation region of the fibrinogen, the extent of this flocculation region had to be determined first: it showed that fresh undialyzed fibrinogen, therefore containing much salt, had a flocculation region of pH 4-pH 9; with pH 4 the fibrinogen migrates toward the cathode and with pH 9 toward the anode. As after isoviscous examinations the blood plasma represents a mixture of the most varying electropositive and electronegative albuminous bodies, it can well be imagined that the

results of the different charges of the plasma colloids guarantees the solution equilibrium of the various bodies which constitute the fibrin. For this reason purely produced and isolated components of the blood plasma were united in different proportions in the expectation of a possible coagulation with fibrinogen. As thrombin is an albuminoglobin mixture, globulin, albumin and fibrinoglobulin were tested, and it was shown that purified, dialyzed solutions (free of even traces of salt) of serumalbumin, serumglobulin, and albumin prepared from white-of-egg produced coagulation with fibrinogen: therefore, in the transition of fibrinogen to fibrin, the electric charge of the coöperating factors may be of importance in the sense of a colloidal discharge.

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**The Coagulation of the Blood in the Thoracic Cavity.**

*M. A. van Herwerden, Nederl. Tijdschr. v. Geneesk., 66:847, Haarlem, March 4, 1922.*

In a previous communication to the journal the author has stated that blood brought into touch with the pleura no longer coagulates. He now reports on experiments made by Henschen, Herzfeld and Klinger on rabbits, showing that blood from the internal mammary artery, which had been made to run into the chest cavity, would not coagulate unless fibrinogen were added. His own experiments give the same result and show that the fibrinogen of the blood is changed into fibrin in the chest cavity.

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**The Nature of the Coagulation Ferment.**

*Richard Stephan, Deutsch. med. Wochenschr., 48:282, Berlin, March 2, 1922.*

All theories of coagulation assume the existence of a specific kinase, the so-called coagulation ferment, which causes the extravascular coagulation of blood. Its absence is characterized by noncoagulation of blood and upon its concentration in the blood depends the speed of transformation of the fibrinogen, and thus the speed of blood coagulation. Klinger classifies it among the proteolytic ferments. In the course of his study of the question of coagulation, Stephan began to doubt the specificity of the coagulation ferment. He even considered it very probable that the control of coagulation was only partly a function of the ferment. An effort was made to establish the identity of the coagulation ferment with an unspecific proteolytic serum ferment. Physical manipulations of the serum (shaking with chloroform) made it possible to disturb its apparent biologic inactivity (*in vitro* it does not develop any typical activity) and to prove the existence of this serum protease in many serums; but its effectiveness intravascularly and in the test-tube is inhibited by the colloidal structure of the serum, the exact nature of which is not quite understood as yet. The carmin-fibrin method permitted the proof by exclusion—as long as it is possible to produce the ferment as such—of the identity of the unspecific tryptic serum ferment with the coagulation-protease. Any reaction produces identical effects upon both of them. Their identity was also proved by observations in spleen irradiation. Their condition is identical in all

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coagulation ferment (hemolytic icterus, pernicious anemia, slow endo-diseases which are characterized by an increase or a decrease of the carditis, cachexia, typhoid condition).

For diagnostic purposes it is important not only to determine the concentration of the coagulation ferment, but also to determine quantitatively the amount of proteolytic ferment, because the blood is more easily coagulated during digestion than on an empty stomach (increase in proteolytic ferment). A permanent increase of the coagulation ferment during a crisis of croupous pneumonia and the considerable increase of fibrinolytic ferment after severe hemorrhage, are both expressions of an increased function of the reticular cell system which produces the ferment, and they are a useful reaction of the organism. The hemolytic function of the spleen system and the production of ferment are interdependent. This shows that the concentration of the ferment indicates the extension of intravital hemolysis.

Therapeutically there is the possibility of increasing the function of all the reticulo-endothelial tissues by means of chemotherapy applied by way of the blood circulation system, and also the influencing of coagulation by spleen irradiation.

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**Influence of Blood Serum on the Coagulative Activity of Tissue Extracts.**

*C. A. Mills and Stewart Mathews, Am. J. Physiol., 60: 193, March 1, 1922.*

While attempting to develop an antiserum for tissue fibrinogen, the authors happened on the unexpected discovery that normal rabbit serum possesses in a marked degree the property of rendering more intense the coagulative action of tissue extracts. This increase (as high as 30 times in one case) was only temporary, later giving way to a decrease in coagulative activity. The determination of the coagulative activity of the extracts was made in all cases by use of citrated horse plasma. In testing the lung extract and serum mixtures, equal amounts of the two were mixed, shaken well and placed in the water bath in which the coagulation tests were being conducted. At intervals, 0.2 c.c. of the mixture was added to the citrated plasma, followed by the proper amount of calcium chlorid and the clotting time taken. It was noted that rabbit serum may markedly increase the coagulative activity of lung extract although the serum itself possesses only about 1% of the thromboplastic activity of the original lung extract. The authors have no theory to offer in explanation of this remarkable property of rabbit serum (and to a less degree, human serum also). It is suggested that many cases of sudden reaction following serum injections may possibly have been caused by the presence of small amounts of tissue fibrinogen (thromboplastin) in the serum, the blood of the patient serving to activate the coagulant to such a degree as to make it effective.

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**Blood Sugar Studies.**

*Max Rosenberg, Arch. f. exper. Path. u. Pharmakol., 92: 153, Leipzig, Feb. 28, 1922.*

This first article is concerned only with a criticism of the methods  
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previously in use, and the conclusions drawn from them. The following sources of error are pointed out: (1) Not only sugar but all reducing substances are determined; this is particularly unfavorable in retention of reducing nitrogen substances. (2) The experiments are made with total blood, not with plasma (Bang's microbe method); but, as experience has shown, there is often a lower value in plasma than there is in total blood; normally the sugar value in the plasma is higher than in the total blood. (3) The normal values of blood sugar are difficult to fix; they seem to have been higher since the war. The conception of a threshold value is difficult to grasp, as hyperglycemia is sometimes observed in normal men without glycosuria; in beginning diabetes there may be normal blood sugar values with glycosuria, and in old cases of diabetes, high blood sugar values without glycosuria. These facts will be explained if, instead of a simple disturbance, a partial function of the kidney, it is assumed that the kidney only secretes those substances from the blood which have no further use in the body. On this hypothesis the threshold value is not a fixed figure, but shows individual time variations.

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#### A Micromethod for the Determination of Sugar in Small Amounts of Blood.

*H. O. Pollock, and W. S. McEllroy, Am. J. M. Sc., 163:571, April, 1922.*

A micromodification of the method of Folin and Wu is described for the determination of blood sugar in 0.2 c.c. blood, which may be obtained from the finger or lobe of the ear. The method has been found to be of value for clinical purposes in supplementing the original method, when blood cannot be obtained from a vein. The solutions are the same as those used in the original method. With an accurately calibrated pipette, 0.2 c.c. blood is drawn and thoroughly mixed with 3.8 c.c. water in a centrifuge tube. Then 0.5 c.c. 10% solution of sodium tungstate is added and thoroughly mixed, and next 0.5 c.c. 0.66 N sulphuric acid; after this the tube is stoppered and shaken thoroughly, and the mixture is centrifuged. Subsequently, 3 c.c. of the clear solution is pipetted off into a Folin blood sugar test-tube, and 2 c.c. of the standard sugar solutions containing respectively 0.2 and 0.4 mg. dextrose is added to 2 similar tubes, together with 1 c.c. water; 2 c.c. alkaline copper solution is added to each tube. Tubes with slightly larger bulbs than those described by Folin must be used. The tubes are heated for six minutes in a boiling water-bath, and are then transferred to a cold water-bath and allowed to cool, without shaking, for two or three minutes. Then 2 c.c. molybdate phosphate solution is added to each tube. The unknown is diluted with water to the 12.5 c.c. mark, and the standard tubes to the 25 c.c. mark. Comparison, in colorimeter cups in the usual way, is made with the standard that comes nearest to the unknown. For higher concentrations the unknown also should be diluted to 25 c.c. The 3 c.c. of solution taken for analysis represents three-fifths of 0.2 c.c. or 0.12 c.c. whole blood. The calculation is therefore made as follows, the proper value of the standard depending upon whether the unknown is diluted to 12.5 c.c. or to 25 c.c.: the reading of standard ÷ reading of unknown, multiplied

by the number of milligrams dextrose in the standard, times  $100 \div 0.12$ , equals the number of milligrams dextrose in 100 c.c. blood.

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**A New Colorimetric Method for the Determination of Plasma Proteins.**

*Hsien Wu, J. Biol. Chem., 51:33, March, 1922.*

Author has devised a new colorimetric method which he believes is much simpler and fully as accurate as any of the other methods. There are 2 steps in the determination of the plasma proteins: (1) their separation from each other; and (2) their quantitative estimation. In the first step the author followed the procedure of Cullen and Van Slyke, with slight modifications. In the second step he made use of the color reaction of proteins with phospho-18-molybdictungstic acid (phenol reagent.) Protein in solution react with this reagent, due largely to the tyrosin which they contain. No experiment was made to determine what the color produced by the proteins quantitatively represented. But since this chromogenic value is a constant for any given protein, the intensity of the color produced under definite conditions can be used as a measure of the amount of the same protein. For the standard a solution of tyrosin was used prepared by dissolving 50 mg. of tyrosin in 250 c.c. of 0.1 NHCl. It was found for human plasma that 1 mg. of tyrosin equals 16.4 mg. of fibrin, 25.2 mg. of globulin, or 27.5 mg. of albumin. In the author's method, the fibrin and the albumin are determined directly, while the globulin is determined by the difference between the total serum proteins and the albumin. By means of this method all the determinations can be made simultaneously and finished in one hour.

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**Studies on the Amino-Acid Nitrogen Content of the Blood.**

*Seizaburo Okada and Toworu Hayashi, J. Biol. Chem., 51:121, March, 1922.*

Previous workers have shown that the amino-acid content of the blood of fasting animals is fairly constant for each species. Under special conditions, however, certain deviations from this constant may take place. The purpose of this paper is to study the conditions under which these deviations might develop. Experiments were carried out on animals and on the bloods of various ward cases. To control the results and to get further explanations a study was made also of the content of blood sugar, urea nitrogen, and nonprotein nitrogen. The authors studied the physiologic amino-acid nitrogen content of the blood; the relation between anesthesia and amino-acid nitrogen content of the blood of dogs; the influence of the removal of the pancreas on the sugar and amino-acid nitrogen content of the blood of dogs; the effect of the removal of the thyroid gland of dogs; the effect of removal of kidneys or the ligating of ureters in dogs; the effect on dogs of the hypodermic injection of pilocarpin hydrochloricum; in human beings, the amino-acid nitrogen and corpuscles in the blood of leukemia patients was studied as well as the amino-acid nitrogen content in the

fractions of such blood. The tabulated results show that the amino-acid nitrogen content of the blood of 28 fasting dogs per 100 c.c. varied from 6.33 to 8.79 mg.; that of rabbits was somewhat higher from 7.22 to 10.60 mg. Anesthesia was found not to influence the amino-acid nitrogen content of the blood during the course of eight hours. The thorough removal of the pancreas caused a transient increase of the amino-acid nitrogen in the blood. The increase began within a few hours and lasted for at least two days after extirpation, after which it diminished again even to a subnormal figure. When a part of the pancreas was left under the skin in connection with the blood-vessels, the blood amino-nitrogen remained normal. Neither adrenalin nor pituitrin, hypodermically administered, influenced the amino-acid nitrogen content of the blood. Removal of the thyroid gland and hyperthyroidism gave similar negative results. The ligating of both ureters or the extirpation of both kidneys caused a marked increase of the amino-acid nitrogen, in parallelism with the increase of urea and non-protein nitrogen in the blood. Hypodermic injection of pilocarpin caused an increase of the amino-acid nitrogen content in the blood. From observations on human subjects it was learned that the amino-acid nitrogen content in the blood is increased in leukemia, which increase parallels the number of white corpuscles. The analysis in fractions of the blood in leukemia showed that the white blood-cells contain 6 or 7 times as much amino-acid nitrogen as the plasma.

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**Note on the Ammonia Content of Blood.**

*Thomas P. Nash, Jr., and Stanley R. Benedict, J. Biol. Chem., 51:183, March, 1922.*

This article is a reply to a personal communication from Dr. T. Addis, of Stanford University Medical School, who suggested that the increased ammonia which these authors found in blood of the renal vein on the occasion of recent work, might be due to return of previously excreted ammonia from a kidney which has ceased to function normally under the experimental conditions necessary in drawing the blood. The authors remark that in their animals, except those whose urine secretion was controlled over a definite period, the renal blood was taken as quickly as anesthesia could be effected and the operation performed; the kidney on only one side was exposed, and this disturbed as little as possible; blood was taken from the vein without even a temporary stoppage of the renal circulation. The authors found, without exception, more ammonia in the renal vein than in other blood; this finding was obtained regardless of whether the blood was taken early or late in anesthesia.

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(1e—409)

**The Determination of Uric Acid in Blood.**

*Stanley R. Benedict, J. Biol. Chem., 51:187, March, 1922.*

The author describes the technic of the new method for uric acid determination in human blood as follows: Standard solutions.—The color obtained in the new method from a given quantity of uric acid is so intense that the standard solutions employed have a concen-  
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tration of uric acid considerably below the solubility of uric acid in pure water. For this reason one is able to employ, as standard, solutions of uric acid which are strongly acid with hydrochloric acid. They are prepared fresh once in 2 weeks by appropriate dilution of the phosphate standard solution described by Benedict and Hitchcock. It is desirable to keep on hand 2 standard solutions, one of which contains 0.01 mg. uric acid per cubic centimeter, while the second contains 0.02 mg. uric acid in 5 c.c. of solution. The second standard is the one commonly employed, but the first may occasionally be of service, and is valuable in instances where it is desired to use the Folin-Wu procedure for comparison of results by the old and new procedures. For the preparation of the first standard, 25 c.c. of the phosphate standard solution (containing 5 mg. uric acid) are measured into a 500 c.c. volumetric flask, and the flask is about half filled with distilled water. Then 25 c.c. dilute hydrochloric acid (1 volume of concentrated acid diluted to 10 volumes with water) are added, and the solution is diluted to 500 c.c. This solution contains 0.01 mg. uric acid in 1 c.c. For preparation of the second standard (the one which is most frequently employed) the procedure is the same except that instead of starting with 25 c.c. of the phosphate solution 10 c.c. are employed and diluted after acidification exactly as for the other standard. The blood is precipitated with tungstic acid as described by Folin and Wu, and then allowed to stand from ten to twenty minutes before filtration. The use of excess of acid in the precipitation is to be avoided. Then 5 c.c. of the water-clear filtrate (representing 0.5 c.c. blood) is transferred to a test-tube and 5 c.c. water is added. The standard solution, containing 0.02 mg. uric acid is placed in another tube and the volume likewise made up to 10 c.c. To both standard and unknown are added 4 c.c. 5% sodium cyanid solution containing 2 c.c. concentrated ammonia per liter. To each tube is then added 1 c.c. of the arsenic phosphoric acid tungstic acid reagent. The contents of each tube should be mixed by one inversion immediately after addition of the reagent, and placed immediately in boiling water, where the tubes should be left for three minutes after immersion of the last tube, but the time elapsing between immersion of the first and last tubes should not exceed one minute. After the three to four minute heating the tubes are removed and placed in a large beaker of cold water for three minutes and read in a colorimeter against the standard, preferably within five minutes after removing from the cold water. Employing the standard solution containing 0.02 mg. uric acid and using 5 c.c. of the 1:10 blood filtrate, the calculation for the uric acid content of the original blood is as follows:  $S - R \times 4$  equals the number of milligrams of uric acid per one hundred cubic centimeters of original blood. S represents the height of the standard solution in millimeters, and R the reading of the unknown solution.

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Are the Carbohydrate Groups Detectable during the Acid Hydrolysis of Blood Globulin a Decomposition Product of the Albumin Molecule?

Leo Langstein, Biochem. Ztschr., 127:34, Berlin, Feb. 28, 1922.

In the decomposition of blood albuminoids a sugar was obtained which was identical with d-glucose. On the strength of the quantitative (Sec. 1—Page 988)

estimation or reducing substances the amount of albumen molecules in carbohydrates contained in globulin was taken as 1.4%. The results of the investigation were doubted by Abderhalden, Pergell and others, who assumed the sugar to be an admixture or impurity. Carefully purified globulin preparations were therefore prepared and hydrolyzed with 3% sulphuric acid and in another experiment with 5% hydrobromic acid. From this preparation, which had been purified with extraordinary care and dialyzed for several days, 0.5 to 0.9% reducing substance could, nevertheless, be split off. The admixture of sugar would therefore seem to be excluded.

(1e—411)

**Physiologic Variations of Pepsinemia.**

*Loeper and Debray, Progrès méd., 49:121, Paris, March 18, 1922.*

Pepsin circulates in the organism and is eliminated with the urine. To study its variations in the blood the authors proceed as follows: 4 c.c. serum are obtained under aseptic conditions; 2 c.c. are mixed in a test-tube with 10 c.c. distilled water to which 1 drop pure hydrochloric acid is added. This tube is incubated for twenty-two hours. An analysis is made immediately to determine the quantity of albumin present in the unused portion of serum. The difference between this and the albumin found after incubation represents the amount which was transformed by pepsin. The fact that this transformation is almost completely prevented when the serum is heated at 70°C. for a short time, and that peptones are found in the filtrate of the incubated serum, is a proof that it is really due to the action of pepsin. By using this technic the authors found that the amount of pepsin present in the blood increases regularly after meals, until the second hour, and decreases thereafter. Pepsinemia seems therefore to follow closely the physiological variations of gastric secretion.

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**The Macroscopic Demonstration of Hemokonia (Demonstration of Fat in Blood Serum).**

*F. Glaser and Buschmann, Med. Klin., 18:261, Berlin, Feb. 16, 1922.*

In the diagnosis of icterus and chiefly of its dissociated form, the microscopic hemokonia test, which is difficult to perform, can be replaced by the microscopic examination of blood serum in order to discover opalescence or cloudiness after consumption of a slice of buttered bread (50 gm. butter). This test, for which the name of macroscopic hemokonia test is proposed, can be reinforced if we pour into the test-tube, over the serum, a recently prepared aqueous solution of glycerin (5%). If the blood serum contains fat (in the normal subject two hours after consumption of 50 gm. of butter smeared on bread) there appears at the limiting layer between both fluids, a white ring, best seen after twenty-four hours' sojourn in the incubator at 37° C.

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**The Prevention of Darkening of Acid Hematin in Solutions in the Colorimetric Method of Autenrieth.**

*H. Gram, Acta med. Scandinav., 56:52, No. 1, Stockholm, 1922.*

In the Sahli and Autenrieth apparatus for hemoglobin determina-  
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tion, the test is based on the production of modified hemoglobin, and color comparison with a standard. With the Autenrieth apparatus, transformation of oxyhemoglobin into acid hematin, during the first thirty seconds after mixing with decinormal HCl, is accompanied by a color change from red to brown. Immediately afterward, the mixture darkens. A delay of ten minutes is required before comparing the colors, and minor errors occur through temperature variations, acid concentration and other factors. The author has sought to correct these disadvantages. The solution of the problem is the following: The diluting liquid should consist of 98 parts (c.c.) decinormal HCl plus 2 parts (c.c.) oxydol Petri. Oxydol is a 3% solution of hydrogen peroxid containing infinitesimal amounts of a proprietary organic substance which prevents decomposition. Acid preservatives are not suitable for the purposes of the hemoglobin test. No blood or other foreign matter should be allowed to contaminate the laboratory solution of oxydol. After diluting the blood by the mixture indicated, comparison may be made after three minutes. If the colors are compared considerably after three minutes, no noticeable error is introduced. The objectionable darkening is prevented and no error occurs through changes in room temperature. The apparatus must be standardized by comparison with the regular technic or by a new determination of the oxygen capacity. The Autenrieth test is very accurate. Buyers should compare the color of the wedges provided, with that of an acid hematin solution, in order to be sure that the standard color is correct. Comparisons made with this test should be limited strictly to daylight. This improvement is not applicable to the Sahli test. It has been tried out not only for normal blood, but for blood obtained from a large number of disease conditions.

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**On the Fate of the Amino-Acids Permeating the Red Corpuscles.**

*Keizo Hiruma, Japan Med. World, 2:65, Tokyo, March 15, 1922.*

The results of the author's experiments are in accord with those of Kozawa and Miyamoto, showing that amino-acid markedly permeates the red corpuscles in vitro. The amount of amino-acid permeating the red corpuscles decreases after a certain time. This, it is thought, may be due to the fact that decomposition has, in the meantime, taken place through a ferment in the red corpuscles. The content of amino-nitrogen of the red corpuscles increases after a certain time (five to ten hours). This may be because after a certain time the vitality of the cells decreases and autolysis takes place.

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**The Rapidity of Sedimentation of the Erythrocytes.**

*Richard Ley, Ztschr. f. d. ges. exper. med., 26:58, Berlin, Jan. 20, 1922.*

For a closer investigation into the causes of varying degrees of rapidity of sedimentation of red blood corpuscles, clinical observations  
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and experimental investigations of human and animal blood have been employed. The clinical findings corroborate prior observations.

In contrast to nervous disorders, organic diseases increase the rapidity. In extreme cases of polycythemia and anemia, the number of erythrocytes is not without influence upon the rapidity of sedimentation. Experimental investigations have shown that the temperature is of importance, the optimum of increase being around 37° C., and the most powerful influence between 17° and 37°.

The relations between the rapidity of sedimentation and surface tension were further investigated, the stalagmometer of J. Traube being used. It developed that the rapidity of sedimentation increased with the viscosity of the serum; thus rapidity of sedimentation appears to be a function of the behavior of the albumin bodies of the plasma. At the same time, it represents another link in the chain of evidence showing that the variable rapidity of sedimentation is an expression of the chemicophysical changes in the blood, being possibly the most delicate indicator for the same.

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**Further Researches on the Rapidity of Sedimentation of Erythrocytes of the Same and Different Animal Species and under Different Conditions. II.**

*Emil Abderhalden, Pflüger's Arch. f. d. ges. Physiol.*, 193:236, Berlin, Feb. 9, 1922.

Although chemical analysis reveals great constancy in the composition of the blood-plasma of various animals, specific differences nevertheless manifest themselves by certain signs which can not as yet be evaluated by chemical and physical methods. Such differences include the rapidity of sedimentation of the red blood-corpuscles, which is of added interest from the fact that the alteration occurs under conditions that also govern the production of so-called Abderhalden's reaction. The rapidity of erythrocyte sedimentation is increased during pregnancy if the serum is subjected to dialysis before adding the erythrocytes. Cholesterol accelerates and lecithin retards rapidity of sedimentation, which is of importance in regard to cholesterinemia in pregnancy. Unlike serum or plasma, the chemical composition of erythrocytes varies in different genera, those of the horse, pig and rabbit being free from sodium, while all others show approximately the same sodium content. Closely related species exhibit similar conditions in respect to erythrocyte sedimentation, though no relationship exists in the chemical composition of the erythrocytes. Plasma albuminoids may influence the phenomenon and cholesterol and phosphatids may affect it indirectly through altered conditions of the plasma albuminoids and particularly of the globulins. In connection with these questions the oxygen consumption of erythrocytes under varying suspension stability was investigated, though final results are not as yet available.

A further experimental series dealt with the question whether the suspension stability of erythrocytes in the same blood is uniform. Further, the question arose whether the condition of the plasma albumin is the only determinant or whether there is a determining relation between blood-corpuscles and suspension agent. Experiments seem to indicate that the red blood-corpuscles of an individual are not entirely (Sec. 1—Page 991)

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uniform. Analysis shows that the less the number of erythrocytes, the greater is the rapidity of sedimentation. Therefore, if that portion of the erythrocytes taken from the deepest layer of a blood column obtained by centrifugalization precipitates more rapidly, this can not be explained by an increase of formed elements, as such increase could only effect a diminution in the rapidity of sedimentation. Washed corpuscles precipitate more rapidly the greater the concentration of the saline solution but otherwise they show the same behavior as centrifuged cells. On the other hand the duration of centrifugalization obviously influences the process, so that differences in the physical behavior of erythrocytes may be suspected, even though these are not susceptible of proof. Duration of time alters the rapidity of sedimentation in the same plasma. Experiments on the rapidity in native and foreign plasma show the importance of plasma to the suspension stability of the blood, but the erythrocytes are a codeterminant, as some erythrocyte species precipitate rapidly in any plasma. Erythrocytes undergo certain alterations when placed in a foreign plasma, and their rapidity of sedimentation remains unchanged even after they are returned to their own plasma. However, after washing the erythrocytes in their native plasma, the sedimentation rapidly again approaches the original value. The presence of foreign corpuscles in plasma produces changes in the latter which may be detected optically with the interferometer. As these increase with the duration of stay of the foreign erythrocytes the foreign plasma can not be responsible for the changes, especially as 0.1 c.c. bovine corpuscles exercises a greater influence on horse plasma than 0.1 c.c. bovine plasma.

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### The Influence of Stimulants upon the Rapidity of Sedimentation of Blood Corpuscles.

Hanns Löhr, *Klin. Wchnschr.*, 1:483, Berlin, March 4, 1922.

The rapidity of sedimentation of erythrocytes in normal persons does not show any considerable variations in the course of a day. Intramuscular injections of albuminoids (analogous to the increase of typhoid agglutination by nonspecific stimulants) increase the rapidity of sedimentation, and intravenous injections are still more effective. Colloidal silver preparations (collargol and dispargen) produced the same effects, as well as adrenalin and pilocarpin. Blood transfusion inhibited the rapidity of sedimentation in one case of pernicious anemia, where a considerable increase already existed.

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### The Effect of Venous Congestion upon the Swelling of Erythrocytes.

Josef Aieollo, *Biochem. Ztschr.*, 124:100, Berlin, Nov. 21, 1921.

As the blood is taken from a congested vein of the arm for its chemical examination, it is interesting to note whether changes in the chemical construction of the total blood and in the distribution of the constituents into plasma and corpuscles appear as a result of the congestion. The number of blood-corpuscles is admittedly somewhat increased in the congested blood, as is also the albumin content of the  
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serum and the specific weight, shown by the determination of the dry residue and refraction. The condition of swelling of the blood-corpuscles was also determined according to the method described by Richter-Quittner. The tests showed that the volume of the blood-corpuscule increases somewhat in all the tests; the water content of the total blood decreases; that of the serum is either slightly decreased or remains almost unchanged; that of the blood-corpuscles decreases considerably. On comparing the water content of arterial blood and venous blood (withdrawal of blood without congestion) it was seen that there is no important difference between the capillary, the arterial, and the venous blood, respectively, in regard to the distribution of the water between the corpuscles and plasma. During congestion there is a thickening of the blood and in the majority of cases a loss of water from the blood-corpuscles. In the congested venous blood there is less potassium and fewer total ash constituents than in the uncongested venous blood; these are changes associated with the water content.

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**The Erythropoietic Action of Germanium Dioxid. II. The Source of the Erythrocythemia Produced by Germanium Dioxid in the Albino Rat.**

*Frederick S. Hammett and Joseph E. Nowrey, Jr., J. Exper. Med., 35:507, April 1, 1922.*

In a previous publication it has been shown that germanium dioxide is nontoxic to the mature female albino rat when injected subcutaneously in amounts up to 180 mg. per kilo of body weight. A systematic study was then made of the effect of the compound on the erythrocyte and white cell content of the normal rat blood. It was found that, regardless of sex, a marked and valid increase in the red cells in the circulation followed the injection of relatively small amounts of germanium dioxide solutions. In view of certain gross findings at autopsy of the rats used in these experiments, and because of the persistence of the effect for many days after the injections, it is justifiable to conclude that germanium dioxide is an erythropoietic agent of remarkable potency. This report presents completed evidence on which that belief is based. A histologic comparison of the liver, spleen, bone marrow, circulating young erythrocytes, and differential count in mature male and female albino rats receiving germanium dioxide was made with their litter controls not receiving this compound. The livers of the test animals in most cases showed a condition of capillary dilatation and more erythrocytes were found in these capillaries than in those of the controls. There was no evidence of any red cell formation by the liver. The spleen gave the impression of being slightly more congested and of having a slightly denser concentration of cells in the Malpighian corpuscles than those of the controls. There was no evidence of an increased red cell destruction nor was there any evidence of splenic erythropoiesis. In the bone marrow of the mature rats there was evidence of a marked stimulation in formation of nucleated erythrocytes, in that many more of these cells were found here than in the marrow sections of the controls. The circulating blood contained more young red cells as demonstrated by the increased number of erythrocytes taking the polychromatic stain (Sec.1—Page 993)

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than did the blood of the controls. No noteworthy differences in the values for the various types of white cells in circulation determined by the differential count could be found between the 2 groups.

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**Immature Leukoblasts.**

*L. I. Aquino, Rev. Asoc. méd. argentina, 34:352, Buenos Aires, Nov., 1921.*

Pappenheim believed the myeloblasts to be hemocytoblasts with azurophil granulation. Ferrata considered leukoblasts to be lymphocytes with a more or less myelocytic nucleus. Aquino studied normal and pathologic human hematopoietic organs in various stages of leukemia, and also animal organs. He found that the predominant and common factor of the leukoblast is the initial myelocytic structure of its nucleus; on the other hand, he agrees with Ferrata that the presence of azurophil granules deprived them of their character as indifferent cells. According to Pappenheim the initial lymphocytes, with or without azurophil granulations, give origin to leukoblasts with or without azurophil granulations and myelocytic nuclei. Ferrata believed that the initial hemocytoblasts with azurophil granulations give origin to myeloblasts with hemocytoblastic nuclei and azurophil granules. Aquino is convinced that the original lymphocytes without azurophil granules produce proleukoblasts P with myelocytic nuclei and without azurophil granules, and proleukoblasts F with lymphocytic nuclei and with azurophil granules. Both these proleukoblasts give origin to leukoblasts with myelocytic nuclei and with azurophil granulations.

Proleukoblast P is defined as a cell the nucleus of which, after being lymphocytic, presents the clear picture of a myelocytic structure, with honey-combing and thickening of the chromatin. These cells are surrounded by nucleoles with the appearance of parachromatin; the protoplasm lacks azurophil granulations, is made up of more or less rarefied spongioplasm, in combination with the initial oxyplastic formation, with bioplasm, accumulated mainly in the periphery, and a variable development of the cell body.

Proleukoblast F is a lymphoid cell with a hemocytoblastic nucleus with or without nucleoles, with a leptochromatic structure and an amblychromatic staining power, a nuclein network, giving it a granulated and diffuse appearance, without parachromatic contrast, and with a basophilic protoplasm containing azurophil granulations and a more or less spongioplasmatic structure in accordance with the individual case and the period of evolution.

Aquino concludes that one may designate as a leukoblast any element which represents a myelocytic nucleus and azurophil granulations.

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**A Method of Obtaining Pure Native Human Leukocytes.**

*Wilhelm Starlinger, Wien. klin. Wchnschr., 35:172, Feb. 23, 1922.*

By the described method one can obtain leukocytes from any person without disturbing the native character of the cells. The method is based upon the fact that when the speed of depression of the erythro-  
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cytes is increased, the leukocytes are separated from the erythrocytes by allowing the citrated blood to stand for a while. As an increase in the speed of depression depends upon an increase in the fibrinogen contents of the blood, if this condition does not exist, it can be produced artificially by adding the necessary amount of fibrinogen.

With a paraffined syringe 4.5 c.c. blood is quickly taken from a vein and mixed in a glass vessel with 0.5 c.c. of a 5% sodium citrate solution (already in the glass), avoiding the formation of foam. Within ten or fifteen minutes the red corpuscles drop to the bottom spontaneously, evidenced by the broad layer of plasma that separates by that time. After waiting until about half of the blood column has cleared up, the plasma containing the leukocytes may be collected by means of a pipette and the leukocytes obtained from it. If the red corpuscles do not drop spontaneously within fifteen minutes, the blood is immediately centrifuged, and part of the plasma (now free of leukocytes) is replaced by a solution of fibrinogen. The mixture is well shaken and allowed to stand for about fifteen minutes when the erythrocytes will drop very quickly. The collected plasma still contains numerous erythrocytes. The plasma is again centrifuged, the liquid is filtered off, the sediment is mixed with an equivalent amount of physiologic salt solution (sodium chlorid 0.7, sodium bicarbonate 0.18, potassium chlorid 0.02, calcium chlorid 0.02%) and after that centrifuged once more; the leukocytes now conglomerate and drop to the bottom in small lumps, while the erythrocytes remain suspended for a while longer. The number of leukocytes is so predominant that they agglutinate very easily, while the erythrocytes are so few in number that they remain separated. The agglutinated leukocytes can easily be separated again by shaking them with physiologic salt solution.

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**The Distribution of the Leukocytes in the Circulation.**

*Otto Stahl, Deutsch. med. Wchnschr., 48:314, Berlin, March, 10, 1922.*

All observers agree that even the slightest physical disturbance of any nature may cause a considerable change in the number of the leukocytes. These disturbances may be the inspiration of irritating substances, change in posture, myogenetic digestion leucocytosis and psychic influences.

Blood was removed from the lobe of the ear and from larger vessels with a record syringe. The count was made with a Thoma-Zeiss apparatus and Zappert counting lines. A high leukocyte count was found as a result of anesthesia and after operation. It was also found that there were more leukocytes in the cutaneous capillaries than in the larger vessels. Although the limit of error is usually assumed as 3.6-9%, and the difference in the count of the blood of the capillaries and of the large vessels (3%) was within this limit, the author thinks his theory is borne out by the fact that the blood of the capillaries in three-fourths of the cases had a higher count. The laws of movement of fluids in tubes probably explain this difference in the number of white cells in the capillaries and in the deeper vessels. The law of Poiseuille-Helmholz says that the movement of the fluid is slowest

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along the wall and most rapid in the center of the stream. The circulation may be compared to a series of cylinders of fluid which are placed one in another. The middle moves most quickly. The specifically lighter bodies are forced toward the periphery, the heavier ones into the axial stream. The red cells have a greater specific gravity than the white cells. The latter also stick to the wall more easily. The number of leukocytes in the marginal current increases if there is slowing or stasis of the current, a condition easily occurring in the fine network of the skin. The supplying vessel does not contain more leukocytes than the one taking the blood away in inflammatory conditions. The focal blood of the skin contains more white cells in these cases than do the larger vessels.

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**The Lipolytic Power of the White Blood-Corpuscles.**

*Friedrich Nees, Biochem. Ztschr., 124:156, Berlin, Nov. 21, 1921.*

According to Bergel, lymphocytosis is to be considered a curative reaction of the body even though insufficient, in such diseases as tuberculosis and leprosy and in the early stage of typhoid fever, in which the lymphocytes through their inherent ferment exert a fat-splitting action upon fat-containing substances, as the tubercle bacilli in tuberculosis, which contain fatty acid, neutral fat and waxlike substances in addition to albumin. He bases his assertion on experiments in which he allowed lymphocytic pus to act upon beeswax (melting point 64° C.) at 52° C. with the result of a central dimple formation and liquefaction around it; on cooling, a wall-like, raised border remained in the region of the dimple formation. With purely leukocytic staphylococcus and streptococcus pus, not even the slightest change occurred in the wax plate. As a subsequent proof of the fermentive action of lymphocytes, experiments were conducted to determine how leukocytic pus behaves toward fatty substances, upon which the lymphocytes exert their digestive action: for this purpose, beeswax, mixtures of fat and wax, and fat and paraffin, and also such mixtures colored with methyl red were used and kept in an incubator on an average of twenty-four hours at 39-43° C. and in some cases at 52° C.; the pus used had the most varied origins of leukocytic and lymphocytic nature; staphylococcic and streptococcic pus was also used.

Experiments showed that Bergel's method with wax plates is absolutely applicable to test the presence of fat-splitting ferments in the white blood corpuscles. The technic was somewhat modified: the pus was allowed to act upon a mixture of two-thirds lard and one-third wax colored with methyl red. The idea, that a fat with a low melting point, near that of the body temperature, is more easily influenced, was the starting point. The most favorable temperature, different from that of Bergel, was found to range between 30° and 40° C., which finds its explanation in the fact that the leukocytic ferments show less resistance to higher temperature than the lymphocytic ferments. The fat-splitting action of the lymphocytic ferment was confirmed; it is still undecided whether it should be credited with a protective power in Bergel's sense. As the leukocytes also have lipolytic power, which is no less than that of the lymphocytes, it seems to be a general property in regard to the power of splitting fat.

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**The Relation of Blood-Platelets to the In Vivo Agglutination of Bacteria and Their Disappearance from the Blood Stream.**

*Carroll G. Bull and Clara M. McKee, Am. J. Hyg. 2:208, March, 1922.*

The object of this investigation was to study the relation of the blood-platelets to the agglutination of bacteria in the blood stream of animals having an artificial bacteremia, and the part which these elements of the blood play in the abrupt disappearance of bacteria from the circulation. The general technic was to inject into the ear veins of rabbits from 2 to 5 c.c. of bacterial suspensions of suitable densities. Specimens of blood for microscopic observation and culturing were taken from the heart at intervals varying from five seconds to two hours after the injections. Wright's method was used satisfactorily in the platelet counts. The animals were "deplateletized" by the intravenous administration of an antiplatelet serum which was prepared by giving guinea-pigs 3 or 4 intraperitoneal injections of the washed platelets from 50 to 60 c.c. rabbit blood.

From the detailed description and protocols, it appears that both in the immunized rabbits and in the normal animals having natural agglutinins, the bacteria injected into the ear veins are immediately agglutinated and leave the blood stream. It was demonstrated that the association of the platelets with the bacterial clumps is merely incidental, since the agglutination and disappearance of the bacteria from the circulation are not perceptibly modified by their presence. The agglutination and disappearance of the bacteria goes on just as completely and rapidly when the platelets are absent. In these experiments *Bacillus typhosus*, *B. dysenteriae* and *Staphylococcus pyogenes aureus* were used. When the latter was injected into normal rabbits, the individual organisms were not agglutinated, but most of them rapidly left the blood stream. When the platelets were present they collected into columns to which many of the cocci became attached before leaving the circulation; but when the platelets were not present the cocci left the circulation with equal rapidity. In this case the bacteria left the blood stream because the plasma so altered them that they adhered to the endothelial cells of the capillary systems. Virulent pneumococci remained in the blood stream because they were neither agglutinated nor opsonized. It may therefore be concluded that depending upon the antibody content of the blood, one of 3 things occurs when artificial bacteremias are produced, viz.: (1) the bacteria are neither agglutinated nor opsonized, and continue to circulate in the blood stream; (2) the bacteria are agglutinated, or are both agglutinated and opsonized, and rapidly leave the circulating blood and collect in the capillary systems of the liver, spleen, lungs, etc.; or (3) the bacteria are not agglutinated, but are opsonized and rapidly leave the circulating blood and likewise collect in the internal organs.

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**Two Cases of Total Inversion of the Viscera.**

*P. Menetrier and P. Isch-Wall, Bull. et mém. Soc. anat. de Paris, 18:512, Dec., 1921.*

One case was that of a woman of 26, the other that of a man of 80. In the first instance, the patient died of pulmonary tuberculosis. Autopsy was possible both in the patient and in her child 2 months of age, in whom the visceral arrangement was normal, suggesting that inversion is not regularly transmitted. The woman's right lung had only 2 lobes, the left had 3; the heart was inverted, with the aortic ventricle on the right and in front; the pulmonary artery and the aorta crossed each other in the reverse of the usual manner. The liver was in the left hypochondrium, the spleen in the right. The suprarenals were reversed; the cecum and appendix were in the left iliac fossa. The intestines as well as the lungs were the seat of numerous tuberculous lesions. In the second case, in which death was due to uremia the stomach was inverted, with the greater curvature on the right; the ileum crossed the body from right to left, and the cecum was found on the left side under the small inverted liver; its appearance was infantile, and the appendix extended from left to right. The descending colon, after its descent on the right, was obliged to make a sharp turn; it then ran transversely across the spinal column and ascended again on the left side at the posterior wall, toward the cecum. The large intestine thus made a complete circle; then turned downward again at an acute angle and passed to a normal rectum. The heart and lung showed various abnormalities. There was a single kidney of horseshoe type, and multiple spleen. It is to be regretted that cases of total inversion of viscera are practically never discovered except at autopsy. Radiologic and electrocardiographic examinations might in these 2 cases have revealed facts of great interest. Several illustrations are given.

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**An Abnormal Bilateral Supraclavicular Muscle.**

*E. Olivier and J. Braine, Bull. et mém. Soc. anat. de Paris, 18:486, Dec., 1921.*

The muscle extended from the posterior border of the clavicle to the manubrium. It was situated in a reduplication of the sheath of the sternomastoid. Its origin covered the internal third of the posterior clavicular border. Its fibers were thin and long. The thin and flat terminal tendon was about 1 cm. wide; it crossed the anterior sternoclavicular ligament without adhering to it, and was inserted on the upper, external and anterior surface of the manubrium.

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**Peculiar Iron-Containing Myelin Masses Found in the Lungs.**

*R. Nissen, Beitr. z. path. Anat., 70:212, Jena, Feb. 14, 1922.*

In a patient 46 years old, who died from peritonitis due to perforation, histologic examination revealed in the lungs nodular masses of the

supporting connective tissue, which peripherally consisted of leukocytes, and at the center contained giant cells of the type of foreign-body cells. Wherever found, they surrounded peculiar central myelin-like stratified masses which stained dark blue with hematoxylin and showed a variable, doughy form. Often a cavity existed in the center of these masses, filled with long narrow crystals which in the unstained section were colorless and doubly refractive. In a few of the alveoli, fresh fibrinous exudate with very few exfoliated alveolar epithelial cells and some leukocytes could be found. The different microchemic reactions were all negative, save the one for iron. These myelin masses contained an abundance of iron. Apparently, this precipitation of myelin masses is a secondary phenomenon of chronic edema.

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(1f—102)

**Mixed Tumors of the Face.**

*Nikolay Paus, Beitr. z. path. Anat., 70:96, Jena, Feb. 14, 1922.*

The present work deals with the well known salivary gland tumors, known in literature under diverse names. Under the caption of mixed tumors of the face, there are included several tumors of similar structure occurring in the salivary glands, the cheek, the lip, the orbit, or in the throat and the palate. These tumors may be malignant or benign; even the latter may show a recurrence due either to incomplete removal, or to a multiple anlage. Histologically, the tumors consist of fibrillar connective tissue, mucoid tissue, cartilage, bone, fat and lymphatic tissue. The parenchymal cells are not of an endothelial but of an epithelial nature, both squamous and cylindrical epithelium being represented. These tumors must have originated from undifferentiated embryonic cells. In those showing more complicated structure, the inclusion of the germinal tissue must have occurred very early; in the simpler varieties this may have taken place at a later period. There is no sharp limit between benign and malignant tumors. Certain forms of this variety of neoplasms are designated as cylindromas and sarcomas, but for the most part they really belong to the mixed tumors of the face.

It is difficult to give a prognosis from the histological appearance. Good results may be expected from radical extirpation of very cellular mixed tumors, provided it is carried out while the tumors are still in the benign stage. Sooner or later they become malignant, and then the prognosis is bad. The exact localization is of no great consequence in determining their structure—they all originate from extruded embryonal cells in the vicinity of the branchial arches. However, some differences do exist. Tumors in the region of the parotid and of the submaxillary gland are the most complicated, while those of the cheek, orbit, lip, and palate usually show a simpler structure.

Mixed tumors are not limited to the face, but may occur in other parts of the body. Everywhere their structure corresponds to the normal development of the local tissue or organ—in the breast there occur tumors derived from the ectoderm of that region; underneath the skin, there are found epithelial neoplasms formed of the epithelium of the corium and of the cutaneous glands. They form a part of the large group of mixed tumors and teratomas, the most differentiated

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representatives of this group being the true teratomas, and the simplest variety, the dermoid cysts. All are derived from stray embryonic cells, in the sense advanced by Cohnheim.

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(1f—103)

**Studies on Lymphoid Activity. VI. Immunity to Transplanted Cancer Induced by Injection of Olive Oil.**

*Waro Nakahara, J. Exper. Med., 35:493, April 1, 1922.*

It was regarded of interest to determine whether or not the local reaction to oil is accompanied by a general lymphoid stimulation and, if so, the effect on the resistance to cancer inoculation in mice. Commercial olive oil was used in these experiments. Injections were made intraperitoneally, followed by a histologic study of the general condition of the lymphoid organs, with special attention to the number of mitotic figures present as this had been shown to be a fair index of the degree of stimulation. The experiment indicates that the most pronounced reaction in the lymphoid organs followed the intraperitoneal injection of a dose of 0.2 c.c. of the oil. It may be said that resistance to transplanted cancer can be induced by 3 classes of agents: (1) homologous tissue, a biologic agent; (2) x-rays and heat, physical agents; and (3) olive oil, a chemical agent. In the course of the development of the resistance a definite period of latency is detectable following the oil injection, and the maximum degree of resistance appears at about the tenth day. This state of resistance, as has been determined by histologic studies, is preceded by a proliferation of the cells of the lymphoid germ centers and, after the cancer inoculation, is associated with a lymphoid infiltration about the grafts, as well as by a second stimulation of the lymphoid germ centers and an increase in the number of the circulating lymphocytes.

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**A Case of Malignant Ganglioneuroma.**

*Jörgen H. Berner, Beitr. z. path. Anat., 70:203, Jena., Feb. 14, 1922.*

In a girl of 4½, an egg-shaped tumor measuring 13 by 10 by 8 cm. was found retroperitoneally below the spleen and above the left kidney. In the vicinity of this main growth, 7 smaller tumors varying in size from a pea to an almond, were found. The main tumor consisted essentially of ganglion cells and nerve fibers divided by connective-tissue septa. The smaller tumors were lymphatic metastases of the larger. The lymphoid tissue was reduced to small remnants and the growths also contained ganglion cells and nerve fibers, though less abundant than the large mass. Hence this was a ganglioneuroma with well differentiated cells, which had formed true metastases. Clinically, the child had given symptoms of Addison's disease. The left suprarenal body was not found at autopsy; the right appeared normal macroscopically. No microscopic examination was made.

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**Histology of the Pedicles of the Nondematous Portions of Hydatidiform Moles.**

*Hub. Hillebrand, Monatschr. f. Geburtsch. u. Gynäk., 57:67, Berlin, Feb., 1922.*

The author bases his observations on 3 rather old specimens and 3 fresh ones of hydatidiform moles. The pedicles were cut in serial sections and examined microscopically. It was shown that the length varies between 0.1 mm. and several centimeters; the thickness is also variable. Blood-vessels are rarely found in the pedicles, and when present are atrophic. The epithelium is occasionally absent or consists of syncytium alone or in combination with a Langhans layer, showing evidences of hyperplasia, degeneration and necrosis. The stroma of the pedicles is very dense and strong. There seemed to be no difference between central and peripheral pedicles.

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**The Pathologic Anatomy of Influenza with Special Consideration of the Cerebral Changes.**

*Gerhard Mittasch, Frankfurt, Ztschr. f. Path., 26:406, no. 3, Wiesbaden, 1922.*

This study is based on 462 necropsies of influenza cases from July, 1918, to July, 1920. No general predisposition to influenza from previous diseases was made out, and the combination with pulmonary tuberculosis is relatively rare. Pregnancy increases the dangers of infection. Changes in the respiratory tract and lungs were observed regularly, consisting mainly of inflammation and suppuration of the accessory sinuses, and laryngitis and tracheitis, often necrotic. The changes in the lung were characteristic, constituting a "mottled pneumonia." Dark red areas, more or less flaccid and not rarely surrounded by a grayish yellow border, alternated with areas of firmer consistency and of grayish red to grayish yellow color, with some parts pale and acutely distended; more or less extensive subpleural hemorrhages completed the picture. A bloody serous, cloudy fluid flowed in abundance from the mottled cut surface and the air content of the lungs was exceedingly low. Wedge-shaped hemorrhagic foci, which do not represent infarcts, were characteristic. Purulent pneumonic processes, severe diseases of the vessels, and thrombophlebitis of the pulmonary vessels were frequent. As a rule, the pleura was involved and the bronchial lymph-nodes showed an inflammatory or hemorrhagic swelling. The heart frequently revealed degeneration of the myocardium, more rarely myocarditis, not rarely a verrucous endocarditis (always on the mitral valve in these cases). The pericardium was rarely involved. The blood-vessels were not examined systematically. The condition of the spleen depended upon the severity of the secondary and general infections. The kidneys in 45% of the cases showed cloudy swelling, frequently acute hemorrhagic inflammation. The adrenals showed hemorrhages into the cortex and medulla, but no striking loss of lipoid. There were no characteristic changes in the liver and the involvement of the gastro-intestinal tract was slight; the male genitals were not changed, but occasional hemorrhages were found in the uterus.

ine mucosa. In the musculature were found hematomas and the characteristic, light, cloudy coloration of waxy degeneration, especially in the diaphragm, psoas and the thoracic musculature. The changes in the central nervous system consisted of edematous infiltration, hyperemia and hemorrhages into the internal meninges and brain substance; histologically, there were perivascular infiltration and changes in the glia consisting of increased nucleosis along the vessels and changes of the glia cells (shrinking or distension, disappearance of the tigroid marking, neuronophagia). The histologic findings indicate that the influenza encephalitis is an inflammatory process of predominantly hemorrhagic character, but mycotic embolic processes may also occur in general septicopyemia. According to the author's view, the macroscopic and microscopic changes in the brain in (epidemic) lethargic encephalitis (Econo) are not specific or characteristic. The hope of localizing the inflammatory foci in definite centers of the brain has not been realized.

The coincidence of epidemic encephalitis with epidemics of influenza; the frequency of simultaneous influenza and encephalitis in individual cases, and the fact that encephalitis was found with greater frequency in the last influenza epidemics than in any other acute infectious disease, logically leads to the assumption that epidemic encephalitis bears a direct relationship to influenza. The establishment of epidemic encephalitis (lethargic) as an entity is ungrounded. Both hemorrhagic encephalitis and epidemic encephalitis are true inflammatory processes, and there is no basic difference between them, nor can the latter be considered an entity.

The demonstration of the influenza bacillus was rarely possible, but mixed infection was always profuse and evident, a significant element of this mixed infection being a diplostreptococcus. The extraordinary contagiousness of influenza would argue for a specific excitant as the causative agent of the disease in the last analysis. Possibly this primary organism acts only as a pioneer for the elements of the secondary infection, or perhaps it has the effect of increasing the virulence of a simultaneous or subsequent mixed infection. The deeper air passages were always the portal of entry for the virus.

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**Lesions of the Central Nervous System in Typhus Fever.**

*G. Marinesco, Ann. de l'Inst. Pasteur, 36:209, Paris, March, 1922.*

The virus of typhus is neurotropic. All parts of the nervous system may be affected. The symptoms are concordant with the lesions. Lesions of the peripheral and cranial nerves, changes in the central blood and along the peripheral nerves, have been studied in 4 cases. The studies were purely histologic. In sensory, motor and mixed nerves, hemorrhages and the lesions of interstitial neuritis were present. Infiltration is localized in the lymphatic spaces and in the capsules and venules of the interfascicular and intrafascicular connective tissue. The lesions are found in the optic and olfactory nerves, spinal ganglia and nerve roots. The meninges, white substance and gray matter of the spinal cord are considerably affected. The most characteristic cord lesion consists of nodules scattered throughout the white and gray matter of the lumbo-sacral, dorsal and cervical regions. The nodules occur especially in the

posterior horns and Clarke's columns. Lesions of the nerve cells are relatively slight. The medulla is especially affected. Nodules are numerous and infiltration is extensive. Nodules and vascular lesions are found in the choroid plexus. The medullary meninges are involved, and the peduncular meninges are also affected. The nodule formation is absent in the meninges. It is present in the corpora quadrigemina and cerebellum. Cortical lesions are not transmitted by way of the meninges, but, in general, the gravity of the cortical lesions parallels that of the meningeal changes. The virus reaches the central nervous system by way of the blood and lymph and also, as an ascending neuritis, along the peripheral nerves. The lesions also extend by the infected cerebrospinal fluid. Several plates are employed to illustrate the anatomic findings.

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**The Chemistry of Artificial Icterus.**

*Egmont Muenzer, Biochem, Ztschr., 127:214, Berlin, Feb. 28, 1922.*

By means of Ehrlich's aldehyd reagent for the detection of urobilinogen, the most delicate disturbances of liver function may be demonstrated, this reaction being particularly intense in affections attended by the disintegration of blood-pigments. The importance of the aldehyd reaction is illustrated by two patients suffering from artificial cutaneous pigmentation produced by the ingestion of picric acid or its derivatives. With regard to artificial yellow pigmentation it is to be borne in mind that biliary pigment or urobilinogen, or both, are always present in urine in icterus, i. e., a jaundice from liver affection. The tests for urobilin urobilinogen and biliary pigment are best carried out by mixing 8-10 c.c. urine with an equal volume of alcoholic zinc acetate solution. The filtrate is divided into two parts. One part is employed immediately for the urobilinogen reaction, the other being allowed to stand for the formation of urobilin. The filtered residue contains the biliary pigments. It is mixed with a few drops Bouma's reagent (20 parts Obermayer and 20 parts alcohol) when the biliary pigment goes into solution and the filtrate, in the presence of biliary pigment, has a green color.

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**Histologic Changes in Experimental Infection with Leptospira Icteroides and Leptospira Icterohaemorrhagiae.**

*W. H. Hoffman Cron. med.-chir. de la Habana, Jan., 1922, p. 184.*

The changes almost always present in animals which have died of infection with *Leptospira icteroides* are above all pronounced icterus, with hemorrhages of the subcutaneous tissue, especially in the inguinal, axillary and retroperitoneal regions. Hemorrhages are frequently found in the epididymis. They are of special diagnostic significance when they occur, as they always do, in multiple foci in the lungs, but they are found in practically all the organs. The liver and kidneys are congested and icteric. The blood exhibits changes essentially different from those in yellow fever in man. In all the animal experiments, typical blood curves were found, with periodic increase of leukocytes and extensive, rapid destruction of erythrocytes. Hoffman is of the

opinion that these anatomo-pathologic lesions, in animals, due to *L. icteroides* "Merida" of Noguchi, correspond to hemorrhagic septicemias. Many of the lesions suggest a type of bacteriemia found in man and due to the Eberth-Gaffky bacillus: as, for instance, hyaline degeneration of the striated muscles, blood degeneration, phagocytosis of the erythrocytes in the spleen and lymphatic glands, medullary infiltration of the intestines; all of which lesions are mentioned in connection with yellow fever in man.

Evidently the liver changes have not the importance in experimental infection that they have in yellow fever occurring naturally in man. The icterus in the animals seems to be essentially of splenic or hematogenous origin, as the liver changes are not sufficiently serious to account for this symptom. There is no doubt that the histologic changes differ fundamentally from those of yellow fever in man. On the other hand, there is a striking resemblance to the changes found in Weil's disease.

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**The Transmission of Equine Infectious Anemia to Small Laboratory Animals.**

*R. H. Jaffe and F. Silberstein, Ztschr.f.d. ges. exper. Med., 26:104. Berlin, Jan. 20, 1922.*

Infectious anemia has become a menace to the equine stock in some districts, especially since the war, and it is necessary to try every means of recognizing the disease in proper time. The causative agent is unknown and the clinical picture shows little that is characteristic. Therefore, the only definite diagnostic method today consists in the transfer of the disease from a suspected horse to a healthy one.

Rabbits, rats and mice were inoculated intramuscularly, intraperitoneally and intravenously, with blood, liver and spleen pulp from 4 horses suffering from infectious anemia. Rabbits were found to be susceptible and the experiment was carried through 7 animals.

When the course was acute, changes were found in the spleen only. They consisted of a loosening of the malpighian bodies, with granular degeneration of a large proportion of the lymphatic elements. Chronic cases showed an atrophy of the spleen. The liver was of a smoke-gray color; the liver cells were choked with granules which did not give the iron reaction. Fourteen animals died between the twelfth and the ninety-sixth day. Four succumbed in the first week. Apparently, the material inoculated and the number of animals through which the inoculations were carried determine the severity of the infection. Blood and spleen pulp are the best material for inoculation. The rabbit appears a suitable laboratory animal for the further study of this important equine disease, and rabbit inoculations may become a valuable aid in establishing the diagnosis.

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**Degeneration and Regeneration.**

*Paul Ernst, Deutsch. med. Wchnschr., 48:215, Berlin, Feb. 16, 1922.*

*Degeneration.* Virchow differentiates (1) fatty metamorphosis (with atheroma); (2) calcareous and clayey metamorphosis, calcification (Sec. 1—Page 1004)

tion and ossification; (3) pigment metamorphosis, pigment degeneration; (4) softening, coagulation, liquefaction and colliquation; (5) thickening, induration, obsolescence, horny metamorphosis; (6) amyloid and waxy degeneration.

It is important at the present time to examine the nature of the cellular as well as of the physicochemical processes. There is a great future in colloidal chemistry in regard to these biologic questions. There is necrobiosis, death and softening of the various elements in the active and passive processes of degeneration. Micronecrosis is death limited to single cells or cell groups. Fatty degeneration is a type of degenerative disturbance of metabolism, in which there is a breaking up of the substances to nonspecific, neither useful nor harmful substances. Progress has been made by many chemical, physical and microscopical methods in the determination of fat and fat-like substances. These methods showed the nature of physiologic storing of fat, deposit of fat, transport and absorption of fat and the relation to general constitutional disturbances such as poisoning by alcohol, phosphorus, tuberculosis. Local and general adiposity is explained by increased avidity of the cell for fat. Degenerative infiltration means that the damaged cell does not use up the fat which it takes up from the food and the fat remains untouched. There is a close relation between the carbohydrate metabolism and fat. This applies to the storing, transport and retention of glycogen. It is only necessary to consider the relation between the fatty layer, diabetes and lipemia. The progress has not been so great in the study of albumin metabolism. There is no unity of opinion as to the significance of cloudy swelling. It is sometimes possible to demonstrate fine granules of a regressive nature which may be seen by aid of vital stain. This may lead to further advances. Greater progress has been made in mucoid-gelatinous and amyloid degeneration. The knowledge of hyalin and colloid degeneration is limited. Keratin, a product of hornification, is an albuminous body. Hornification depends on the place and time and the degenerative manifestations may regress. Disturbances in the metabolism of minerals is especially distinct in the process of calcification. The cells do not degenerate because the elements become calcified but because they take up more calcium and more iron after onset of degeneration. A change in the colloidal mixture and suspension of calcium in the blood and tissue is known as calcium gout while increase of the calcium content by the food is called storing up or deposit of calcium. Calcification is not of itself a form of degeneration; it may sometimes be an accompanying sign of degeneration as in dystrophic calcification. Pigment degeneration may be considered when the pigment is a sign of the using up of tissue as in old age and marantic states and in deposits of pigment in the muscle of the heart and intestine, testicle, kidney, renal cells. Autogenous pigment is apparently the result of action of oxydases on the products of the breaking-down of albumins (tyrosin, adrenalin,) and which was studied in Addison's disease, ochronosus and alkaptoneuria. The hemoglobin pigments indicates the destruction of the red cells. There are no two cases of degeneration which are exactly alike. Calcium is the index of destruction. The products of albumen degeneration are oxidized and changed to melanin. Albuminous clouding is perhaps only a change in the degree of dispersion of the colloid solution of albumin. Amyloid and hyaline degeneration depend on a fermentative precipitation of an albumin which

was formerly soluble. Degeneration is simply a term to signify a deterioration in all respects. It leads from irritation and excitation to fatigue, exhaustion, paralysis and death. Morphologic changes correspond to the functional failure and the absence of these means that the changes have not as yet been found.

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**Parenchymatous Regeneration.**

*Nathan, Ann. de méd., 11:59, Paris, Jan., 1922.*

The author has obtained parenchymatous regeneration by implanting connective tissue in the parenchyma of various organs. The earlier work was done with bone, which may be restored not only by periosteum, but by any form of connective tissue. Recent studies refer to the liver, kidney, thyroid and peripheral nerve tissue.

The hepatic experiments were made with rabbits. A generous incision is made in the liver, a fragment of omentum with or without a pedicle) is introduced and the capsule then sutured. The animal is killed and examined in six or eight weeks. The connective tissue grafts are found full of nodules composed of hepatic epithelial elements. The cells replace the original trabeculae, and migrate into the spaces of the connective tissue. Collections of hepatic cells extend in loose tissue, finally uniting to form the nodule. In loose connective tissue, the cells group into typical hepatic lobules. The renal studies were made in rabbits and dogs. Results were similar to those obtained in the liver. The same growth of parenchyma is produced in the thyroid of dogs. The sciatic nerve also follows the general law, i. e., parenchyma proliferates in young connective tissue. The process is arrested in adult connective tissue. Certain pathologic tissue changes appear to be aborted efforts at regeneration, as in subacute or chronic hepatitis. The author has also studied compensating lobar hypertrophy of the kidney following diphtheric nephritis. The subject, a child, died of scarlet fever thirteen months after the onset of nephritis. The lack of available connective tissue in the adult human kidney is perhaps the cause of the severity and incurability of nephritis in the adult. Connective tissue grafts probably owe their success to the process described in this paper. The functional capacity of the tissue thus artificially restored has not yet been determined.

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**The Chemistry of Amyloid Degeneration.**

*Hans Eppinger, Biochem. Ztschr., 127:107, Berlin, Feb. 28, 1922.*

During an examination of a case of so-called true amyloidosis the amyloid tumor was removed from the liver parenchyma. Its elementary analysis gave 50.26% C, 7.29% H, 14.79% N, and 3.39% CN. The amount of ash was minimal. Probably this may be an albuminoid, which is also indicated by Van Slyke's analysis. The percentage proportion of carbon to nitrogen is very similar to that in other proteins. The substance is free from phosphorous and sulphur and, therefore, contains no chondroitinsulphuric acid. Amyloid is formed from many amino-acids. The high proportion of tyrosin and the absence of cystin and histidin are remarkable. The substance is rich in diamino-acids and

hence possess a fairly basic character, appears to contain purin bodies, and is apparently free from carbohydrates as far as can be judged by the qualitative tests. That the foreign amyloid was deposited in this case, while the other proteins are built up, is obviously due to the different character of amyloid as compared to the ordinary proteins.

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**Amyloid Tumors of the Mesentery Accompanied by General Amyloid Degeneration.**

*M. Ecoffey, Schweiz. med. Wchnschr., 52:202, Basel, Feb. 23, 1922.*

In the the autopsy on an 85 year old woman, the author observed a general amyloidosis with the formation of two amyloid tumors in the mesentery. Sections of the heart, spleen and liver gave a positive Lugol reaction, while the reaction of the kidney was negative. The mucinous membrane at several points of the intestine showed a positive Lugol reaction. The mesentery contained two yellowish tumors, one measuring 8.5 by 5 by 2.5 cm. and the smaller 2.5 by 1.5 by 1 cm. The tumors were well defined, the surrounding parts of the mesentery being abnormally thick and fat.

The sections of the tumor stained typically with hematoxylin and also by van Gieson's method. Amyloidosis was particularly pronounced in vessels, which also contained calcareous deposits. Annular amyloid masses were also found upon the nerves coursing through the tumors. The lymph-glands imbedded in the tumors were also affected by amyloidosis. The amyloid degeneration of the smaller tumor was farther advanced. In this case amyloidosis was caused by tuberculous peritonitis. The calcification and ossification of amyloidosis were not pronounced, and the giant cells did not show an inflammatory reaction.

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**The Physical Changes in the Tendon Sheath at the Beginning of Wallerian Degeneration.**

*E. A. Spiegel, Beitr. z. path. Anat., 70:215, Jena, Feb. 14, 1922.*

The pathology of wallerian degeneration has been studied in numberless instances. Death of the axis-cylinder in this peripheral part can be explained by the fact that it is cut off from its cell, but it yet remains unexplained why the tendon sheath, which is frequently segmented and entirely interrupted at every node of Ranvier, should undergo degeneration throughout the entire peripheral portion of the severed nerve. The lesion produced by section of the nerve explains only the death of the segment involved as far as the next node of Ranvier; the degeneration of the entire peripheral portion of the medullary sheath is probably caused by processes taking place in the peripheral portion of the axis-cylinder, for the most recent investigations seem to show, both in the traumatic and in the nontraumatic degeneration, that the primary lesion occurs in the axis-cylinder. When a nerve is severed, the factors which produce the difference in surface tension between cell protoplasm and nerve ending are paralyzed, and the axoplasm tends to return to the spherical shape. This is the physical manifestation of wallerian degeneration of the axon. Later the myelin also tends to approach the spheri-

cal form, and the degeneration of the medullary sheath would seem to be the result of diminished surface tension of the axoplasm. Since alterations of pressure within the medullary sheath, depending on surface tension, are shown by a change in the double refraction, this latter phenomenon was examined. It was found that on the second day after severing the nerve, there could be noted a diminution of the double refraction, which remained at least partly reversible up to the sixth day, and can be regarded as the result of swelling. In this connection mention may be made of the question of cerebral swelling. It occurs in company with such processes as are attended by acute lesions of the nerve cells and their processes. Hand in hand with this there must be swelling of the medullary sheaths of the degenerated nerves.

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**Dystopia of the Neurohypophysis.**

*A. Priesel, Beitr. z. path., Anat., 70:209, Jena, Feb. 14, 1922.*

A marked thickening of the infundibulum of the hypophysis was found in a man of 78 years. It consisted of a nodular mass 5 mm. thick and 6 mm. long. Examination of serial sections showed that the portion of the hypophysis located in the sella turcica consisted only of the tissue of the anterior lobe in which accumulations of eosinophile cells had occurred, resembling an adenoma. The nodular structure at the infundibulum proved to be a displaced neurohypophysis. At the boundary of both lobes there existed a sizable cavity. It is assumed that the malformation was due to an abnormally ventral position of the rudiment of the neurohypophysis, which thus developed not behind, but upon the glandular portion.

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**Plasma Cells and Mast Cells.**

*F. Jiménez de Asúa, Arch. de cardiol. y hematol., 3:46, Madrid, Feb., 1922.* ....

Normal and inflammatory tissues obtained from cases of syphilis, tuberculosis and tumor were examined, after Del Rio Hortega's staining method, with ammoniacal silver carbonate had been employed for showing the nuclear structure. The gold chlorid solution should be gently warmed. Granular staining was accomplished with toluidin blue and 5% creosote in alcohol was used for decolorizing. Various other methods were employed for comparison. The perinuclear halo shown by the staining described above does not indicate incipient atrophy. Blue-staining cells may be separated into 4 groups: (1) typical cyanophil cells; (2) cells with flocculent protoplasm; (3) cells with filamentous protoplasm; (4) cells with rarefied protoplasm. Plasma cells are probably derived from the normal lymphocytes of connective tissue. Forms transitional between fixed and plasma cells have not been observed. Plasma cells do not become fixed cells but may represent modifications in function. This is probably the meaning of the several forms. The cells containing flocculent protoplasm may represent a pathologic transformation. The so-called vacuolar or hyalin degeneration, or Russell's bodies, are probably pathologic secretion products. It is impossible to state the function of the plasma cells but it may be assumed to be an important one.

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**SECTION 1—ANATOMY, PHYSIOLOGY AND  
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**SECTION 1. ANATOMY, PHYSIOLOGY AND PATHOLOGY**

**1a. ANATOMY AND PHYSIOLOGY**

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The Anatomic and Functional Differences of the Germ and the Somatic Cell.

*George A. Boyd, Colorado Med., 19:75, April, 1922.*

The chief anatomic difference between the germ and somatic cells is the number of chromatin threads and their antecedents. The fertilized organ is the product of the united complementary halves of the germ cells. Hence comes the sum of the hereditary possibilities of these two. The chief physiologic difference between the germ and somatic cell is that the germ cell is incapable of initiating cell division. The union of the germ cells or the apposition of their nuclei initiates a series of cell divisions in which from the first cleavage division a precise and predetermined relation exists between each generation and the adult part to which it gives rise. This predetermined control is located in the chromomeres of the chromatin threads. The individual chromomeres are relatively as unlike as the parts of the body to which they give rise. As there is a limit to the number and dissimilarity of the chromomeres in the germ cell, so is there a limit to number and parts of the organisms to which they give rise. The measure of this limit is the adult organism. When this limitation is reached, sex is nature's provision for producing a new individual and consists in first coupling the paternal and maternal homologous somatic chromosomes and then redistributing and reducing them so that the germ nucleus carries one-half the number of somatic chromosomes of mixed paternal and maternal origin. In the reduction, one-half the sperm cell loses its sex chromosome and the egg cell one of its two. Union of the sperm cell having a sex chromosome with the egg produces a female, and without the sex chromosome a male. It is possible to alter or destroy the individual chromomeres of sex cells without destroying the body, but not without producing defects. Guyer and Smith have so altered the chromomeres determining the development of the rabbit's lens, by cell cytotoxins produced by injecting chickens with pulped rabbit lenses and injecting the sensitized chickens' serum into the vein of a rabbit ten days pregnant. This change in the chromomere in the offspring of the defective-eyed rabbits thus produced is reflected in similar changes in the lenses of successive generations which seem to follow the mendelian law.

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Studies in Placental Permeability. II. Localization of Certain Physiologic Activities in the Chorionic Ectoderm in the Cat.

*R. S. Cunningham, Am. J. Physiol., 60:448, May 1, 1922.*

This paper records the reaction of the cat's placenta after more extended exposures to sodium ferrocyanid and iron ammonium citrate (Sec. 1—Page 1009)

than those reported in the first paper. The animals used were pregnant cats, in the latter half of gestation. Into the vein of the fore-leg were injected balanced solutions of sodium ferrocyanid and iron ammonium citrate, 1½% of each salt. At the termination of the experiment the animal was killed, the uterus opened and the fluid carefully withdrawn from the amniotic sac with a syringe and needle. The fluid was then tested for the experimental salts. The fetuses were removed and their abdominal cavities opened. If the bladder was distended it was treated as in the case of the amniotic sac. The placenta and membranes were fixed in Bouin's fluid, the acetic acid in the mixture precipitating the Prussian-blue. In the analysis of the amniotic liquid and fetal urine, solutions of ferric chlorid and ferric sulphate were used to test for the ferrocyanid, and ferrocyanid was used to determine the ferric iron. Histologic examination of the placentas of living fetuses from the experiments in which a combined injection of sodium ferrocyanid and iron ammonium citrate was given, showed Prussian-blue surrounding the giant cells in a definite blue ring. The maternal endothelial cells contained a few blue granules within their cytoplasm. The striking finding was the appearance of the syncytium of the chorionic ectoderm. Here the Prussian-blue was precipitated in clumps and fine lines within the cytoplasm adjacent to the maternal endothelium and extended between the nuclei. The border of the chorionic ectoderm adjacent to the fetal vessels always remained free of the Prussian-blue. In most of the experiments having a duration of more than eight hours there was evidence of some precipitation of Prussian-blue in the living placenta. The author remarks that it is evident from the experiments that the precipitation of the Prussian-blue granules indicates the course of the sodium ferrocyanid and the iron ammonium citrate through the placental tissues, and that the latter salt under consideration is in some way arrested or changed during this passage so that it does not enter the fetal circulation in such a form that it can be detected by the reactions used. The author suggests that the chorionic ectoderm has the power of altering the chemical structure of this compound (iron ammonium citrate) and that one stage in this process results in the change of the iron ammonium citrate in such a way that a compound is formed which would combine with the sodium ferrocyanid and form Prussian-blue. This is proven by the fact that longer exposure of animals that had received a single dose given at the beginning of the experiment show increasing amounts of the Prussian-blue formed during life.

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**The Origin of the Motor Neuroblasts of the Anterior Cornu of the Neural Tube.**

*Raymond A. Dart and Joseph L. Shellshear, J. Anat., 56:77, Jan., 1922.*

The foundation of His's conception lies in the ectodermal or neural tube origin of motor neuroblasts. This paper aims, to demonstrate the origin of these motor neuroblasts from the myotomes and to establish the principle of both functional and structural continuity between the nervous system and the other systems which it controls. The term "effector" refers to the motor neuroblast (or neurone) and the term

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"expressor" refers to the organ acted upon by the effector neuron, be it muscle or other structure. As evidence of coöordinated activity the authors submit their observation of movements of a coöordinated character with abduction and adduction in embryos before the appearance of sensory neuroblasts and when the apparent relationship between the neural tube and the myotome is one of contact. Paton in 1906 observed that the primitive movements of abduction and adduction of the body begin at a time when these phenomena "may as yet neither be designated as myogenic or neurogenic in origin." If the His conception is correct there is at this stage no connection whatever between the neural tube and the myotomes. The effectors are in the neural tubes and have not yet grown out to the expressor organ. How then are there coöordinated movements of abduction and adduction? The authors say that from our present knowledge of the origin of sensory neuroblasts, of the constitution of the neurones, and the primitive neuro-epithelial and neuromuscular cells, it is evident that to establish His's conception, the demonstration of some pathologic-like lesion is logically necessary, but even then the presence of coöordinated movements of abduction and adduction would be entirely unexplained.

The authors present several section drawings of *Squalus Acantias* at various stages of development, one showing the relationship between the myotome and neural tube to be one of contact, and others showing protoplasmic continuity between the myotome and neural tube. The beginnings of the division of the effector-expressor mechanism of the myotome into its 2 components, effector and expressor, can also be seen. The remaining figures show the further changes in the myotome and region between the myotome and neural tube. These figures illustrate the banking up to the nuclei lying in the protoplasm between the neural tube and the myotome. If histologic evidence be the criterion, these figures clearly point to a centripetal rather than a centrifugal movement, for the neuroblasts are outside the neural tube in the early stages and inside in the later stages although no explanation of the relative change in position of the motor neuroblasts is offered by His.

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**The Development of the Skull under Normal and Pathologic Conditions.**

*Hedda Weinnolt, Beitr. z. path. Anat., etc., 70:311, Jena, March 11, 1922.*

The author opposes Thomas' views on the interstitial growth of bones and the normal development of the skull, in which the pressure of the growing brain is distinguished from that of the intracranial fluid. In one case, in which the brain had remained at the stage of the solitary vesicle, and therefore represented a vesicle distended by fluid, it was found that the cranial bones were normally developed. In anencephalia, every developmental influence of the brain on the cranial bones is evidently abolished. But all the cranial bones are distinctly recognizable, although their relation and form vary from the normal skull. It may be inferred from this that under normal conditions the increased tension at the poles of pressure does not initiate the development of the cranial bones, but that another cause must be present.

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According to Roux's theory, the first anlage of organs and tissues is due to inherited properties of the organism, and function is then super-added as a formative factor. The concept of function should be here defined as the histomechanical use of the cranial bones. The author's observations also tend to disprove the opinions of Thomas about the normal ossification of cranial sutures. On this question, the following conclusions are drawn: (1) Intracranial pressure causes tension on the cranial bones and therefore on the suture substance; it causes chiefly tangential tension. (2) The tangential tension is increased by the traction of muscles, the latter acting vertically on the sutures. (3) The tension in the suture tissues is so great that ossification of these tissues really should set in. This is inhibited by movement along the line of the suture produced by muscular traction, which though insignificant is quite powerful as compared to the narrow line of the suture. (4) The resistance or the material tension of the suture tissue is increased by the formation of Sharpey's fibers (instead of ossification) until it suffices for the purpose. (5) Sharpey's fibers are only found in the direction of the greatest tension, that is, they are mostly directed tangentially. (6) The normal condition is the persistence of open sutures. The ossification of sutures in old age results from the diminution of the brain size and of the radial tension. (7) As exceptions to these laws are the synostosis of certain sutures found in early youth in all members of the same species, thus in man, the frontal, and the transverse and sagittal occipital sutures.

In cranial deformities with normal intracranial pressure a distinction must be made between cases with pathologic synostosis of the sutures and those with normal sutures. The latter include the deformities in scoliosis and caput obstipum, influences exerted upon the skull by posture in infancy, plagioccephaly due to prolonged sojourn of the head in the pelvic strait before birth, and cranial changes due to rickets and osteomalacia.

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### The Structure of the Vertebrate Head.

*W. B. Primrose, Glasgow M. J., 97:223, April, 1922.*

For over a century it has been supposed that the vertebrate head was formed by the fusion of a number of metamerie segments. It is now possible to show that this supposition is not supported by morphologic facts. On the contrary, these facts go to show that the head is entirely formed by the first metamerie segment. On considering the evolution and the development of the apparent metamerie segments, it soon becomes evident that no less than 4 morphologically different and distinct skeletons are developing in the head at the same time. These are: (1) the notochord or neural skeleton; (2) the sclerotome skeleton; (3) the facial skeleton; and (4) the splanchnic skeleton. As each of these is determined by a different arrangement of special structures, it follows that none of the parts of any one skeleton can be homologous with any of the parts of another, and there is at once exposed the fallacy of the belief in the homology supposed to exist between the mandible, which is facial skeleton, the hyoid arch, which is sclerotome skeleton, and the thyroid and subsequent arches, which belong to the splanchnic skeleton. Each of these skeletons is destined

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to support structures derived from different fundamental tissues—facial for epiblastic, sclerotome for mesoblastic, and splanchnic for hypoblastic structures, respectively, and all at different times in evolution. Anatomic series can determine no homology. The metamerized mesodermic segment of myotome fails to form any muscles in the head on account of its inability to adapt itself to head-structure and functions. The unspecialized, unsegmented mesoderm in this region can adapt itself to any form of skeleton, and it actually provides all the specialized muscles of the head. These arise as stalked buds from the dorsal wall of the splanchnocoele.

No individual cranial nerve is able to establish itself as a homologue of a segmental spinal nerve; it is only part of one. The segmental artery of the head is the common carotid. Investigation denies the aortic arches the importance with which they have been credited. They are not homologous with the segmental arteries. The organs of special sense are all developed in the tissues of the face, and belong to the facial portion of the head segment. When the first segment of the body (head) fails to develop there is a deficiency also of all the parts developed in connection with it.

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**The Myodome and the Trigeminofacialis Chamber in the Coelacanthidae, Rhizodontidae and Palaeoniscidae.**

*Edward Phelps Allis, Jr., J. Anat., 56:149, Jan., 1922.*

According to Sensiö the ramus ophthalmicus profundus issues from the cranial cavity through a canal that traverses the dorsal portion of an anterior process on either side of the median bone that he considers to be a basisphenoid. This anterior process forms the lateral boundary of the fossa hypophyseos, and the external opening of the profundus canal lies ventral to the dorsal end of the basipterygoid process of the basisphenoid, and unquestionably ventral also to the surface of articulation, with that process, of the so-called palatobasal process of the palatoquadrate. The nervi trigeminus and ophthalmicus lateralis are said to issue through an incisure at the base of the posterior edge of the basipterygoid process, and the rami maxillaris and mandibularis trigemini presumably to pass outward behind that process, or over its posterior part, in a lateral direction. The ophthalmicus lateralis is said to run over the process, close to the lateral wall of the brain case, and the vena jugularis to have a similar course. This course for the vena jugularis seems improbable to Allis. (1) Such an extremely dorsal course would be most exceptional for this vein. (2) There is practically no room for its passage dorsal to the basipterygoid process in either Wimania or Macropoma, the dorsal end of the process being, in each of these fishes practically in contact with the dermal bones of the roof of the skull. (3) As the hyomandibula is evidently of the teleostoman type, the vein must have passed internal to it, and to have reached that position after passing dorsal to the so-called basipterygoid process, and hence morphologically external to the articulating process of the palatoquadrate, would require a course so devious and indirect that it is wholly improbable. The vein must accordingly have a more ventral course and pass internal to the process of the palatoquadrate. The latter process could not then be a palatobasal one, and if it has

its homologue in any process of the palatoquadrate of recent fishes, that process must be either the otic process of the Dipneusti, or the processus muscularis of the Selachii, Holostei and Teleostei. The wide distribution of the latter process, together with the facts that the process of the Coelacanthidae ossifies as a piscine metapterygoid bone and that it articulates with the cranium in the postorbital region, all indicate that it is a processus muscularis. With the interpretations of the conditions in the Palaeoniscidae, described by Stensiö, this author's work does not agree. According to Stensiö the vena jugularis, running posteriorly, probably enters the anterior end of the so-called myodomic part of the postorbital cavity, but soon turns upward into the trigemino-facialis part, the latter part of the cavity lying between the ascending process of the parasphenoid and the lateral wall of the sphenoid. The further course of the vein is not given, but as the so-called trigemino-facialis chamber has no posterior opening, the vein must, in Stensiö's opinion, either run posteriorly external to the ascending process of the parasphenoid, or enter the cranial cavity through the foramen trigeminum. Allis believes the latter of these assumptions is improbable; and if the vein passed external to the ascending process, the latter process would necessarily be similar to that in Cottus and Amiurus and would correspond to the inner wall of the pars jugularis of the trigemino-facialis chamber of other fishes instead of to its external wall. This is in itself improbable and is furthermore contrary to the homology proposed by Stensiö. The vein must accordingly pass internal to the ascending process, and this assumption is confirmed by a comparison with the conditions in Polyodon, a fish more closely related to the Palaeoniscidae than either Cottus or Amiurus. In Polyodon the vena jugularis traverses a canal in the cranial wall that has been described as the facial canal (Bridge 1879). The nervus facialis issues from the posterior opening of this canal, accompanied by the vena jugularis, and before entering the canal the latter vein receives a branch from the pituitary body. The ganglion of the nervus trigeminus lies largely within the cranial cavity, and the several branches of the nerve pierce the cranial wall slightly anterior to the anterior opening of the facial canal. These conditions so closely resemble those described by Stensiö in Birgeria that it seems practically certain, the author believes, that the so-called myodomic groove or fossa of the latter fish is simply a part of a jugular canal similar to the facialis canal of Polyodon.

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**Odontologic Essays. IV. Relation between Reptilian and Mammalian Teeth.**

*L. Bolk, J. Anat., 56:107, Jan., 1922.*

The simplest mammalian tooth is believed to have evolved from a very simple prototype which must be sought for in reptiles since they are regarded as the ancestors of the mammals. The concrescence theory implies that a mammalian tooth is homologous with several reptilian teeth, resulting from the concrescence of a varying number of simple conical reptilian teeth. The differentiation theory considers that every mammalian tooth, even the most complicated, represents a single reptilian tooth, the originally simple conical crown becoming complicated by the superaddition of the new cusps. The special nature of the food (Sec. 1—Page 1014)

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and the relative position of the tooth in the jaw are regarded as the stimuli determining the growth of the new cusps.

The author's view as to the origin of the mammalian tooth is intermediate. He believes that the reptilian tooth from which that of the mammal evolved was not of a simple conical or styloid form, but had a crown with 3 cusps and a main cone with anterior and posterior accessory cusps upon its sides, placed anteroposteriorly. Every mammalian tooth is homologous with 2 reptilian teeth, the outer half of the mammalian tooth with the series of buccal cusps representing one of these teeth, the inner half with the series of lingual cusps representing the other. These 2 parts may be distinguished as the protomere (buccal part) and the deuteronere (lingual part). The mammalian tooth is believed to have evolved from 2 reptilian teeth, not by means of a real coalescence of 2 separate and independent elements but in consequence of a concentration of the anlage of 2 reptilian teeth. The elements of a mammalian set of teeth are morphologically and genetically equivalent. The terms monocuspidate and multicuspidate possess only a descriptive-anatomic value and do not indicate morphogenetic differences. The differences in shape are solely of a quantitative nature. The anlage of every tooth possesses the potentiality of developing all the cusps found in the most complicated tooth of the set. Complication is to be regarded as completeness. Simplicity of a tooth is explained by the fact that the anlage of a tooth develops its potentialities in a more or less incomplete manner.

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**The Spines of the Cervical Vertebrae and Their Muscles in the Lemuridae.**

*H. von Eggeling, Anat. Anz., 55:201, Jena, March 15, 1922.*

After describing the spinous apophyses of the cervical vertebrae and the musculature of the back and neck in Primates, the author describes the corresponding elements in the Prosimians. In these the spinous apophyses of cervical vertebrae are, as a rule, unforked. The length and the form of the vertebral column, the length and form of the various spinous apophyses vary markedly in different species.

In Lemuridae, Arctocebus, Perodicticus and Lorisinae, the spinous apophysis of the axis is generally very simple, whereas in Tarsius Galago and Indris it becomes generally forked at its extremity. The spinous apophyses of the other cervical vertebrae are forked only in Galago and in this way they are somewhat similar to those of man.

Examinations of muscles could be performed only on some Lemuridae. The transverse spinal muscle is very little differentiated. In these animals, the movements of the cervical column must not have much variety and anatomy in the various segments, so that here also the absence of differentiation in the semispinal muscle and the absence of development of the short interspinal muscles are found with the very slight forking of the spinous apophyses of the cervical vertebrae.

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**Embryogenesis and Morphogenesis of the Joints.**

*Giulio Faldino, Chir. d. org. di movimento, 6:1, Bologna, Feb., 1922.*

Histologic examinations were made of the various joints in a fetus  
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3½ months old which presented multiple adhesions between the joints and the trunk and serious deformations of the lower joints. Believing that only a certain rudimentary degree of differentiation of the articulations was owing to hereditary factors, and that all beyond this was the result of traction and action of the single muscles, Faldino attempted to verify this hypothesis upon the embryo, in which abnormal adhesions immobilized certain joints, and abnormal deformations changed the physiologic muscular forces.

The adhesions arose at a very early period in the development of the embryo; in fact, the connective tissue which constituted them was differentiated and lacked the ectodermal covering at those points where the joints were fixed to the trunk. The differentiation of the various tissues of the body was normal (corresponding to the age of the embryo). The study of the joints showed that those not immobilized by adhesions, and composed of nondeformed segments (shoulders and elbows), were normally differentiated. The joints near the adhesions (wrist) were much less differentiated than they should have been normally, and those where there were adhesions (metacarpophalangeic and phalangophalangeic) were almost entirely without differentiation. In the latter, the contact surfaces were almost flat or only partially curved, and the cavities were outlined only laterally, while in the normal embryo of the same age, the articular cavity is already open and the normal epiphyseal curvatures are already formed. The joints formed by seriously deformed segments (knee, tibiotarsal) were either almost undifferentiated or were constituted in an abnormal fashion. These observations sufficiently demonstrated that the development of joints is, in the very first stages of differentiation, dependent upon philogenetic factors, but, in the later stages, it is related to mechanical factors, first in importance among which is the function of the muscular apparatus.

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**Correlation between Habit and the Architecture of the Mammalian Femur.**

*G. de M. Rudolf, J. Anat., 56: 137, Jan., 1922.*

With the purpose of studying the architecture of the upper end of the femur and the relationship which it bears to the habits of its owner, coronal sections were made through the upper ends of femora of various animals. The human femur was taken as the standard. Comparison of 19 figures suggests a definite correlation between the habits of the animal and the structure of the proximal portion of this bone. If the upper limit of the great trochanter is above the level of the upper surface of the head of the femur, the animal is able to jump or leap. The use of the hind limbs for swimming is also apparently associated with a high great trochanter. Flattening of the superior surface of the head of the bone appears to be associated with the receiving of relatively great stress on this surface. The thickness of the walls of the femur depends upon 3 factors: (1) the amount of cancellous tissue present, this varying inversely as the thickness of the walls; (2) the intensity of the stress and strain acting on, and through, the femur and (3) the histologic structure of the bone.

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The Development of the Saccus Endolymphaticus in *Rana Temporaria* Linné.

Beatrice Whiteside, *Am. J. Anat.*, 30: 231, March 15, 1922.

The material for study consisted of larvae of *R. temporaria* Linné and the investigation was conducted chiefly by means of a series of 30 sections, 6 representing the first stage and 4 each of the following stages. The larvae were first narcotized with ether, the gut extracted, and they were then fixed in sublimate for twenty-four hours. As the author wished to pay special attention to the lime contents of the saccus, decalcification was not attempted, thereby rendering section-cutting very difficult. In order to make the preparations more fit for sectioning they were allowed to remain in 70% alcohol for twenty-four hours, in 95% for thirty-six hours, and in 100% for twelve hours. A little cedar oil was then added to the 100% alcohol, the quantity being gradually increased. After four hours, the larvae were placed in pure cedar oil, in which they remained four weeks. They were then put into 100% alcohol for two hours, into xylol for one hour, into xylol-paraffin for two hours, into paraffin at 40° C. for eighteen hours, and finally into paraffin at 58° C. for six hours. The best stains were obtained by a combination of hemalum with picric acid. In a study of numerous sections of larvae as well as of young frogs in early and late stages of development, one observes first the comparatively late differentiation of the saccus endolymphaticus. In a larva of 4 mm. length, whose auditory organ is in an advanced state of development, the saccus endolymphaticus is present only as a slight expansion of the distal end of the ductus. At a time when all the morphologic parts of the labyrinth are recognizable, this structure is still a small sac, adhering to the roof of the fourth ventricle. The further development of the saccus proceeds very slowly. First an increase in length takes place in a craniocaudal direction, until the saccus reaches from the hemispheres into the region of the seventh vertebra, the saccus of one side remaining separated, however, from that of the opposite side. Next there develops, in a larva 12 mm. long, the processus ascendens anterior, soon followed by the joining of the partes spinales and the first indication of the processus ventralis. The processus ascenden posterior appears at the beginning of the metamorphosis. At the time of its first appearance, the saccus endolymphaticus is an undivided sac lined by a single layer of epithelium. It soon becomes partitioned into 2 tubuli which later subdivide into smaller ones. During the course of development the saccus is divided more and more into small tubuli until it finally has the appearance of a glandular structure. The histologic structure of the cells lining the saccus endolymphaticus remains practically the same during the whole period of development. The calcareous contents of the saccus exist almost from the very beginning. Throughout the entire course of development, no part of the saccus endolymphaticus suffers retrogression, its development being a slow, continuous, and direct one. The author believes, therefore, that it is certain that the saccus endolymphaticus of the frog does not represent a larval organ.

In her admittedly incomplete summary on the structure of the ductus and saccus endolymphaticus in vertebrates, the author remarks

that if one compares the anatomic structure and the relative size of the saccus endolymphaticus in the various classes of vertebrates one sees the following interesting course of development: The saccus is present in all vertebrates, at first as a slight dilatation at the end of the ductus, then as a large vesicle, and finally in the Anura and Ascalabotae as an enormous sac lying in the cavum crani and the vertebral canal. From this maximum of development, the size of the saccus begins to decrease and at last returns in the Mammalia to a hardly perceptible enlargement at the end of the ductus.

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**The Development of the Cloaca in Birds, with Special Reference to the Origin of the Bursa of Fabricius, the Formation of a Urodeal Sinus, and the Regular Occurrence of a Cloacal Fenestra.**

*Edward A. Boyden, Am. J. Anat., 30:163, March 15, 1922.*

This study originated with the discovery by Boyden of a temporary foramen in the dorsal wall of the cloaca, the phenomenon being observed in over 30 embryos. Further investigation revealed that this particular foramen is constant in its mode of development and occurs invariably not only in chick embryos (where it was first observed) but in duck and pheasant embryos as well. It is of special interest because it is probably the only instance in the differentiation of a hollow organ in which a gap occurs in the epithelial wall as a normal and constant feature of development, and also because it enables one, by virtue of the landmarks it establishes, to determine for the first time the exact point of origin of the bursa of Fabricius. In following the origin and fate of this particular foramen, designated as cloacal fenestra, the entire chain of events in the development of the cloaca, from the formation of the primitive streak to the period of histologic differentiation is reviewed.

The formation of a temporary sinus, placed athwart the main axis of the cloaca, has been interpreted as a repetition of the dorsal bladder of reptiles. Boyden calls attention to the regular occurrence in chick embryos of an accessory bursal diverticulum, probably arising from the irregularities consequent upon the formation of the cloacal fenestra. By means of this diverticulum it has been possible to define the primordium of the bursa more accurately than has hitherto been done and to offer new suggestions regarding its phylogenetic origin.

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**A Rare Deviation in the Course of the Innominate Artery.**

*Paul A. Jacusch, Anat. Anz., 55:138, Jena, Feb. 14, 1922.*

In the thorax of a man 68 years of age was found, in addition to adhesion of the pleura of the right superior and middle lobe and a remarkably elevated diaphragm, an innominate artery which arose slightly to the left of the medial plane from the aortic arches, ascended straight up the trachea as far as the thyroid gland and then deviated to the right at a right angle. Its further course followed the gland, which was slightly compressed by it, up to the edge of the right lobe and from

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there a little further in an upward direction where it divided into its terminal branches. The division lies at the upper margin of the clavicle at the height of the transverse process of the eighth cervical vertebra. The artery is 7 cm. in length and is traversed and slightly indented on its anterior surface by the left innominate artery. The cause of this course of the artery does not seem to be due to mechanical reasons induced by the adhesions, but to the fact that it is an enormously long vessel which is fixed relatively at its ends and, therefore, compelled to adopt an arched form. Although the case is an extremely rare one it is, nevertheless, of importance to tracheotomy as no tracheal ring lies free in this variation.

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**Culture in Vitro of Embryonic Tissue of Mammalia.**

*Nikolaus Chlopin, Klin. Wchnschr., 11:628, Berlin, March 25, 1922.*

Pieces of intestine, kidney and extremities of rabbit embryos of various ages were cultured in a hanging drop. This showed the extraordinary plasticity of the embryonic tissue, the rich content of prospective potencies and the marked sensitiveness to external influences. It also shows the tendency for the tissue to exclude itself from external conditions and also to spread into the surrounding net of fibrin. The epithelium is always sharply demarcated from the mesenchyma and is changed in various ways. The mesenchyma may be differentiated further in vitro. Cartilage of young embryos may continue to develop but that of older embryos degenerates.

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**The Effect of Various Salts on the Outgrowth from Experimental Amebocyte Tissue near the Iso-Electric Point and with the Addition of Acid or Alkali.**

*Leo Loeb and Kenneth C. Blanchard, Am. J. Physiol., 60:277, April 1, 1922.*

In this investigation (which is a continuation of preceding work) the authors studied in vitro the effect of solutions of various neutral salts on the cultures of experimental amebocyte tissue with and without the addition of variable amounts of acid and alkali. After preliminary experiments had demonstrated that cells may show very active migration in such acid solutions, sometimes surpassing those in neutral solutions, it was found that through addition of both acid and alkali to neutral solutions not only could an extremely marked improvement in the outgrowth of the amebocytes be obtained, but that the outgrowth in acid may even surpass in extent and duration the outgrowth in Limulus serum which represents the natural and most favorable medium for the migration of the amebocytes. Furthermore it was demonstrated that solutions of neutral salts, which are an unfavorable medium for the amebocyte tissue, may be converted into a favorable one by the addition of acid and, although less strikingly, by the addition of alkali. In carrying on this investigation the authors prepared experimental cell fibrin (amebocyte) tissue of Limulus and placed small pieces of this tissue on cover glasses. The pieces were surrounded with fluid

and the cover glass inverted over a hollow glass slide and fixed to the latter with vaselin. The authors then studied the effect of Limulus serum; the effect of isotonic solutions ( $m/2$  and  $5/8\text{ m NaCl}$ ); the effect of the addition of acid and alkali to the isotonic NaCl solution; the effect of alkali ( $\text{NaOH}$  solution in varying strengths); the effect of acid and alkali in hypertonic NaCl solution; the effect of acid and alkali in combination with  $m/2$  and  $m/4$  solutions of  $\text{LiCl}$ ; the effect of the addition of acid and alkali to isotonic ( $5/8$  and  $1/2\text{ m}$ ) solution of  $\text{KCl}$ ; the effect of addition of acid and alkali to hypotonic ( $m/3$  and  $m/4$ ) solutions of  $\text{KCl}$ , the effect of isotonic and hypotonic solutions of  $\text{RbCl}$  and  $\text{CsCl}$ ; the effect of acid and alkali in combination with  $\text{RbCl}$  and  $\text{CsCl}$ .

As a result of these experiments, it was learned that at the iso-electric point, amebocytes are least resistant to injurious influences and have the greatest degree of permeability to the surrounding fluid. Acid, and to some extent alkali, may protect the cells not only in isotonic but in certain cases also in hypotonic and in hypertonic solutions. Under the influence of the acid in optimal concentration the cells, their consistency, the character of pseudopods, and the movement of granoplasm remain healthy. This relation between consistency of protoplasm and character of pseudopods and ameboid movement is in agreement with the authors' previous experimental results. The authors assume that acid prevents the surrounding fluid, salts as well as water, from entering the cells. In hypertonic acid solution an increase in consistency occurs resulting in an increase in the average sharpness of pseudopods. The acid may not prevent the withdrawal of fluid from the cells in hypertonic solutions, yet to some extent it protects the cells against the entrance and effect of injurious constituents of the surrounding medium. The same protective influence is noticeable to a much greater degree in isotonic and hypotonic solutions. Both acid and alkali exert specific effects, acid hardening and alkali softening the cells. The results obtained with organic acids indicate that the effects observed in acid solution do not altogether depend on changes in H-ion concentration, but that the anion may also play a certain part. In both acid and alkaline solutions the amebocytes may be active. It is probable that various kinds of cells and tissues differ in their sensitiveness to acid and that a greater concentration of neutral salts undoubtedly counteracts certain injurious effects of acids. Those cells are presumably better able to withstand injurious effects of acid which are better adapted to higher osmotic pressures of the surrounding medium.

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**A New Method for the Demonstration of Reticulate Fibers.**

*Rudolf Maresch, Wien. klin. Wchnschr., 35:270, March 23, 1922.*

Equal parts of a concentrated solution of picric acid in methyl alcohol and of a like solution of methyl green, mixed together and placed in a glass cylinder, which can be well closed, serves for preparatory staining of the tissues. The sections of tissue are dried on the slides in the usual way, freed of paraffin, treated for a short time with absolute alcohol and placed for ten minutes or longer in the methyl-

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green-solution. It is recommended that the absolute alcohol be washed with a few drops of methyl alcohol as there may be a strong precipitate from the methyl alcohol solution when it comes into contact with ethyl alcohol, which is not such a good solvent for the dye. The preparation is then rapidly washed in water, and becomes a bright yellowish-green in color. A few drops of a 0.5% aqueous solution of acid fuchsin are added and allowed to act for five to ten seconds. The fuchsin is removed with water or, better, with blotting paper. Dehydration with absolute alcohol follows until the violet-stained section becomes pale greenish-violet in color. The section is then cleared in xylol and mounted in balsam.

A well-stained section shows nuclei of violet color due to the methyl-green and acid fuchsin; the plasma is more or less pale red; acidophil granules are yellow; basophil, intense dark red; and erythrocytes are green. Coarser collagenous bundles of fibers are violet-red. Reticulate fibers are bright red to the finest ends while glia fibers stain a pale red.

The advantages of this method are its constant usability and the fact that the other tissues are stained at the same time as the reticulate fibers. The stain tends to fade after a time but the section can be stained again.

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#### **The Physiology of Olfaction.**

*Antonio Martín Calderín, Siglo méd., 69: 365, 395, Madrid, April 8, 1922.*

To some extent, odor depends on the chemical composition of the odorous substance, but still more on the changes that occur in the sensory cells. There is first a reaction between the odorous substance and the watery, mucous layer covering the cells, but the main reaction occurs between the odorous principle and the lipoids of the cell. The capacity to develop odor depends on the solubility of a substance in water and oil, and on the olfactory power of the cell. Instead of pure water, a 0.73% NaCl solution is employed. This corresponds to the watery layer covering the cells. A temperature of 37.5° C. is slowly raised to 38° C. Castor oil is used for the oil-solubility tests, since its solubility reactions are about the same as those of cholesterol, lipoids, and lecithin. With oil, the temperature should not exceed 37° C. The olfactory power is measured with Zwaardemaker's olfactometer. The tests are begun with alcohols. Ethyl, methyl and other simple alcohols are almost odorless, the higher alcohols possessing odor. Ethyl and methyl alcohol mix well with water, but not with cell lipoids. The small quantities that enter the olfactory cells are destroyed by the cellular defenses before the sense of odor can be developed.

Cetyl alcohol is but little soluble in castor oil, and still less so in saline, the author's figures being 0.00006 per 100. It has therefore practically no odor. Of propyl alcohol, only 2 parts per 1000 are soluble in castor oil, but the alcohol has an odor. This fact depends on a diffusion coefficient much greater in vivo than in vitro. The dependence of odor on solubility extends to isomers of the various substances tested. Alcoholic ethers of indefinite solubility in castor oil, and with an average

solubility of 7.7 per 100 in saline, have odors. Benzol compounds become gradually odorless, as their solubilities diminish (resorcin, 1 per 1000, hydrochinon, 2 per 10,000, phloroglucin, 4 per 10,000). Lack of odor does not always mean total insolubility, but a solubility insufficient to start the olfactory stimulus. The result may be due to defensive action by the cellular constituents, especially the lipoids. The diffusion coefficient must also be sufficiently high, if the sensation of odor is to be produced. Cellular reactions, as well as solubility, play a part in the production of odors, as is shown by the differing olfactory capacities of acetone and methyl alcohol, whose solubility in water, saline, and castor oil, is about the same. By means of diagrams, the author indicates that odorous capacity is increased in substances slightly soluble in water, but highly soluble in lipoids; diminished in substances highly soluble in water, but slightly soluble in lipoids; and absent in substances but slightly soluble in either water or lipoids. Substances highly soluble in both water and lipoids will naturally be strongly odorous.

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**Frequency of the Heart Beat and the Quantity of Blood Delivered Per Minute.**

*Carl Tigerstedt, Acta med. scandin., 56:510, no. 4, Stockholm, 1922.*

The author examined the effects of slow and rapid heart beat in dogs. The volume of blood delivered by the heart per minute was not affected, provided the heart beat was not slowed by more than about one-third its rate. If the frequency is lowered beyond this point, the volume of blood delivered per minute is diminished. If the beat is abnormally rapid, the period of diastole is shortened, dilatation is less complete, the amount of blood delivered per beat is less and as soon as the frequency increases sufficiently, the volume per minute falls. Provided the central veins contain an abundant supply of blood directed toward the heart, the volume of blood delivered per minute is independent of the beat within a considerable range, as indicated above. The ability of the heart (auricle) to expand in diastole, and the power of the ventricle to force blood along, are limited. If the beat is too frequent the auricle cannot be sufficiently filled.

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**Proof of the Occurrence of a Heterotopic Partial Auricular Tachysystole in the Mammalian Heart.**

*Bruno Kisch, Ztschr. f. d. ges. exper. Med., 26:327, Berlin, March 6, 1922.*

In a rabbit narcotized with morphin, in which both vagus and cervical sympathetic nerves had been divided, the pericardium was opened and partial electrocardiograms taken of 2 portions of the right auricle. The electrodes were placed 4 mm. from the heart and 12 mm. apart. After the heart had been observed some time and entirely normal electrocardiograms obtained, an intense auricular tachysystole set in suddenly in which, however, mere inspection failed to disclose incoördination

tion. An immediate cardiogram gave an auricular frequency of 450 per minute. The partial electrogram of the portion more distant from the sinus showed alteration. Therefore the alteration was induced not merely by the high frequency but also by a special disposition of the respective cardiac portion, as the other auricular portion showed normal notch elevation with the same frequency. Before commencement of auricular tachysystole, the notches were diphasic. Monophasic ones, rapidly following each other, were interpreted in one case as partial contractions inasmuch as after a pause (during an extrasystole) first a diphasic and then only rapidly recurring monophasic notches followed. The occurrence of the extrasystole with high frequency is explained thus: Owing to the partial contraction, a part of the auricular musculature remained asystolic and was therefore predisposed to form the starting point for heterotopic stimulation. Specially interesting is the fact that when brief attacks of auricular tachysystole again occurred on further decline of the heart, the partial electrocardiograms yielded curves that were wholly independent of each other and not disturbed by current-loops, from which it is concluded that tachysystole was restricted to a portion of the auricle while the other portion beat more slowly. These attacks lasted one second during which 8-9 auricular contractions were counted. Consequently a frequency of 510 per minute existed in a portion of the auricle. Herein the notch-form of this portion was altered. The other portion showed normal notch-form and a frequency of 4.5 per second. As no relations can be constructed between the 2 cardiac portions the phenomenon must be termed partial auricular tachysystole.

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**Auriculoventricular Dissociation Induced or Interrupted at Will.**

*E. Wertheimer and L. Boulet, J. de physiol. et path. gén., 19: 480, no. 4, Paris, 1922.*

Barium chlorid is injected into the dorsal lymph sac of the frog. The quantity employed is usually 1 cg., more rarely 2 cg. The stimulus consists of a strong induced current, applied to the auricle, septum, or ventricle. The reactions are recorded by Marcy's apparatus. A single induction shock, in a frog treated with the barium chlorid as described, dissociates the normal auriculoventricular rhythm. The abnormal rhythm may consist of 2 auricular contractions, followed by 1 contraction of the ventricle. Another shock restores the normal rhythm. It is probable that the first shock precipitates automatic contraction of the ventricle in a condition rendered previously favorable by the barium chlorid. The second shock renders the ventricular tendency latent. The mechanism of these changes appears to be nervous rather than muscular.

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**The Pulse in the Portal Vein.**

*H. Feil and D. D. Forward, Am. J. Physiol., 60: 312, April 1, 1922.*

In these studies the experimental animals were anesthetized dogs. Through the gastrosplenic branch a small curved cannula was intro-  
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duced into the portal vein, the open end of this cannula being turned toward the splanchnic capillaries. On the insertion of the cannula the gastrosplenic vein had to be tied, thereby causing congestion of the spleen and a small portion of the stomach. Although within the lumen of the portal vein, the cannula, because of its small diameter, interfered but little with the passage of portal blood. Simultaneous records of the heart sounds and the abdominal aortic pulse were taken. The cannula in the portal vein was rigidly connected to a wiggers' optical manometer covered by light rubber dam in order to make it more sensitive. From a study of the curves obtained one learns that a portal pulse consisting of 2 waves is produced in the portal vein during each cardiac cycle. The first wave, *b*, the authors interpret as due to extraneous impact and traction, the second or real wave, *d*, as due to the changing balance which occurs between inflow and outflow of the portal system, at different times of the cardiac cycle. The authors' interpretation of the *d*-wave is as follows: Following each systolic injection a certain pulse volume reaches the splanchnic vessels. Owing to the splanchnic resistance there is a delay of 0.02 to 0.07 seconds in the transference of this increased volume to the portal vein. The portal pressure begins to rise later than the aortic pulse because of this interval. This transfer of blood does not cease with the end of systole but continues into diastole, consequently portal pressure reaches its maximum relatively early in diastole. At this stage, the splanchnic inflow exactly equals hepatic outflow and wave *d* has reached its summit. Thereafter outflow exceeds inflow and portal pressure declines. The amplitude of the chief or *d* wave is determined by: (1) the length of diastole; and (2) the pulse volume entering the portal vein. The latter is determined by the systolic discharge of the left ventricle and by the degree of splanchnic constriction or dilatation.

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**A Comparison of Waves of Blood Pressure Produced by Slow and Rapid Breathing.**

*Robert T. Trotter, Philips Edson and Robert Gesell, Am J. Physiol., 60:500, May 1, 1922.*

Synchronously with the phases of normal respiration, changes in the blood pressure occur, which appear as waves in continuous blood pressure records. Each wave is completed during a single respiration, the rise and fall having a definite relation to inspiration and expiration. These effects of respiration were compared with changes in blood pressure produced by respiration at a rapid rate, using as a basis of study the observation that respiration, approximating closely the rate of heart beat, elicits long oscillations of blood pressure resembling those described above. The experiments supplying the bulk of the data were made on man. Simultaneous tracings of blood pressure, respiratory movements, and time in seconds or fifths of seconds were recorded. Respiration was traced by means of a recording tambour connected with a pneumograph. Continuous blood pressure records were obtained by means of an Erlanger sphygmomanometer. The well known changes of blood pressure occurring during a single respiration, which are more or less synchronous with the changing respiratory phases, are termed simple cardiorespiratory waves to distinguish them from the waves

produced by rapid breathing. The oscillations of pressure elicited during rapid breathing by the interference method are designated as cardiorespiratory interference waves. The most striking difference in the respiratory relations of the simple and interference waves is that in the first the blood pressure changes are complete within the period of a single respiration, while in the second the gamut of the blood pressure changes is run in the interval of several respirations. The production of interference waves depends upon the establishment of cardiorespiratory cycles, in which the number of respirations is greater by 1, or less by 1, than the number of heart beats making up the waves and occurring in the same time interval. Whereas in the cardiorespiratory interference waves the highest and lowest pressures were associated approximately with the beginning of expiration and of inspiration in the simple respiratory waves these relations were reversed. While not assigning the responsibility for the production of interference waves to any particular respiratory factor, the authors incline to the hypothesis that they are primarily due to the changing intrathoracic pressure accompanying respiration.

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Blood Pressure Responses to Hypersystolic Compression of Tissues.

*K. A. Martin and H. L. White, Am. J. Physiol., 60: 323, April 1, 1922.*

In studying the effect of smoking on blood pressure the apparatus employed consisted of air-tight aluminum jackets covering the hand and about two-thirds of the forearm. A rubber cuff fastened to the proximal end of the jacket made a tight junction between jacket and upper forearm. Air pressure was applied in the jackets and piston recorders were connected with them through an Erlanger sphygmoscope to record the oscillations of the pressure. The principle that a rise in blood pressure manifests itself by an increase in the amplitude of pulsations transmitted through a cuff set in the neighborhood of systolic pressure, and by a decrease in the amplitude of pulsations transmitted through a cuff set in the neighborhood of diastolic pressure, the reverse occurring in connection with a fall of blood pressure, was observed. The method of procedure in the first set of experiments was to take the subject's blood pressure by the auscultatory and graphic methods, the Erlanger instrument being used. The pressure in one jacket was then set about 10 mm. Hg above systolic and that in the other at about or a little below diastolic. Then the subject smoked a mild cigar for about thirty minutes. The compression was maintained and pulsations recorded for about ten to twenty minutes after smoking was discontinued. During the course of the record the blood pressure was taken at about five minute intervals by the auscultatory and graphic methods. Both smokers and nonsmokers served as subjects. In every case a rise in both systolic and diastolic pressures was obtained which was manifested by: (1) an increase in the amplitude of the oscillations from the jacket set above systolic pressure; (2) a decrease in amplitude of the oscillations from the jacket set below diastolic pressure; and (3) the findings of the auscultatory and graphic blood-pressure determinations.

The authors later eliminated the question of the effect of smoking  
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on blood pressure and studied the effects of compression only, using a special form of apparatus illustrated and described. Here only one jacket was used and oscillations from it were not recorded, the jacket serving merely as a compression chamber. The authors were able to show that the blood pressure rises to overcome a local ischemia produced by compression of extracranial tissue and that this rise is not accompanied by vasoconstriction in a plethysmographed arm. The authors were unable to obtain any significant changes in blood pressure as a result of brief periods of kidney compression in either anesthetized or decerebrate animals.

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**The Effect on Arterial Hypertension of Increased Fluid Intake.**

*J. B. Orr and Ian Innes, Brit. J. Exper. Path., 3:61, London, April, 1922.*

In an investigation at the Aberdeen laboratories on the influence on protein metabolism of a sudden increase in the amount of water passing through the system, the results suggested that the increased ingestion of water affects the metabolism of protein in such a way that the formation of pressor substances is reduced. A series of experiments was therefore undertaken to determine what influence an increased water intake has upon the blood pressure. In a preliminary control period of two or three days many systolic and diastolic readings were made in each experiment. During this period the normal amount of water was taken. Then for one or more days a measured amount was taken either at one time or at intervals. On the following days, on which the readings were continued, the usual amount of water was again taken. The experiments were thus divided into three periods prewater, water and postwater. For obvious reasons fixed hours of taking the readings were adhered to. One subject was on a constant weighed diet while the others were on a diet that was constant but not weighed. Muscular exercise and emotional disturbances were eliminated so far as possible. Readings were taken after the subject had been allowed to lie on a bed for fifteen minutes, with a Riva-Rocci instrument with Oliver screw compressor, by the auditory method.

Experiments were conducted on (a) 2 healthy subjects with normal blood pressure, (b) 2 subjects with pressure above normal, but kidney lesions lacking, and (c) 14 pathologic cases with markedly raised pressure. The results showed a decrease in blood pressure in the apparently normal subjects and in the pathologic cases after ingestion of water. In the pathologic subjects there was a tendency for the pulse rate to rise on the water days. On the postwater days it fell below the level of the prewater days. In all the subjects the pulse rate was slower after the ingestion of water. The fall in pressure may be due to the elimination of pressor substances that cause arterial constriction. These results are in agreement with Hay's original observations.

A review of the work which has been done on the influence of water-drinking on protein metabolism suggests that 3 factors may be involved in the reduction of blood pressure noted in the experiments. The initial flushing-out process, as evidenced by the increased excretion of nitrogen, may remove pressor substances from the system. Fowler and Hawk's results suggest that anaerobic disintegration of nitrogenous

material in the large intestines may be diminished, with a consequent reduction in the formation and absorption of pressor substances. Substances producing arterial contractions may arise in sluggish or perverted metabolism or under conditions of protein surfeit. The acceleration of the metabolism of protein with the more rapid formation of innocuous final products would lead to the elimination of these pressor substances.

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**Vasomotor Responses Obtained by Slow Interrupted Faradic Stimulation of the Thoracic Sympathetic Nerve.**

*Loyal E. Davis, Am. J. Physiol., 60: 560, May 1, 1922.*

In adult cats anesthetized with urethane the brachial nerves in one extremity were isolated and prepared for stimulation of their central ends. The carotid artery was prepared for blood pressure tracing and the vagi nerves were divided. A tracheal cannula was inserted and air supplied automatically at intervals corresponding to the normal respiratory rate. The thorax was opened and the splanchnic nerve and lower portion of the thoracic sympathetic trunk were exposed. Central stimulation of the lower end of the thoracic sympathetic nerve of the cat by a slowly interrupted faradic stimulus elicits a rise in blood pressure; a similar stimulus of the brachial nerves causes a drop. The synapses in the visceral afferent pathway of the spinal cord of the cat are easily broken down by slowly interrupted faradic stimuli of moderate or weak strength resulting in a pressor response.

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**The Formation of Bilirubin in a Surviving Spleen Outside of the Body.**

*Z. Ernst and B. Szappanyos, Klin. Wochenschr., 11: 614, Berlin, March 25, 1922.*

In order to determine whether bile pigment could be formed elsewhere than in the liver, experiments were performed with an isolated spleen of a dog through which blood was artificially circulated. The spleen was washed by forcing defibrinated blood through the splenic artery. A mixture containing free hemoglobin was then circulated through the spleen. This mixture was free from bilirubin. Blood tests were made in the intervals and the diazo, Hammarstan and Gmelin reactions were performed. There were traces of bilirubin at the end of the first hour and much was present at the end of the fourth hour. The fatty tissue in the hilus of the spleen showed icteric coloration at the end of the test. The bilirubin which was formed in this way was about one-seventh of the quantity excreted by the liver of an animal, and this splenic function in a live animal is even greater. Other elements of the reticulo-endothelial apparatus have the power to form bilirubin. This may be true of every endothelial cell which would mean that large quantities of bilirubin may be formed by these elements in addition to that formed by the liver.

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**Mastication and Digestion.**

*Franz Schütz, Ztschr. f. Hyg. u. Infectionskr., 95: 279, Berlin, March 20, 1922.*

To investigate the trituration of the food in the mouth, according to the method of Gaudenz, cooked food was divided into mouthfuls. Each mouthful was chewed until small enough to be swallowed, it was then expelled and the mouth thoroughly washed out with distilled water. The number of individual particles in the solid portion of the food was determined by means of sieves placed one above the other, of 2.5 mm. and 1.5 mm. mesh. Digestive conditions were studied with good and with poor mastication, the latter produced by means of inserted plates. The division of the food and its solution are incomplete and the filtrate is lessened if teeth are lacking. With defective mastication, the stimulus for swallowing does not come as speedily as otherwise; tongue, cheeks and gums are called into greater play for crushing and mashing the food, and fatigue of the muscles of mastication results. In consequence there is a premature swallowing of insufficiently triturated food, the stomach and intestine become overburdened, and the appetite is impaired.

The value in mastication of the bicuspids and molars, if the wisdom teeth be ignored, is in the ratio of 6:6:12:12. If the total masticatory surface of the bicuspids and first 2 molars be regarded as 100, assuming that the corresponding right and left teeth above and below are of the same size, the values for the individual teeth are 4:2 for every bicuspid and 8:3 for every molar. While the teeth are smaller in the female than in the male, the proportions of the masticatory surface of each individual tooth is the same in both sexes. There are 2 types of mastication force: (1) the practical, about 30-80 kg., and (2) the absolute, about 400 kg. The absolute force has no practical significance. The utilization of food by the stomach and intestine was determined with good and with bad mastication. It was shown on simple bread feedings, the influence of mastication was surprisingly slight, but on a mixed diet, poor mastication caused a definite falling off in the digestion of food with deficient metabolism. This impairment, however, was not very great. In mastication, the area of functioning tooth surface is of predominant importance. The masticatory force compensates for the value of the tooth only slightly and only under normal conditions. The intestinal tract possesses the ability of increasing utilization of poorly divided food, habit playing its rôle. The significance of defective mastication seems to lie in impairment of assimilation from psychic influence.

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**The Gastrin Theory Put to Physiologic Test.**

*A. C. Ivy and J. E. Whitlow, Am. J. Physiol., 60: 578, May 1, 1922.*

The gastrin theory maintains that food substances in contact with the mucosa of the pyloric antrum cause the formation of a hormone, gastrin, which is absorbed into the blood stream and carried to the glands of the fundic mucosa stimulating them. In order to study the

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physiology of the pyloric secretion, animals with 2 gastric pouches, one a Pavlov pouch and the other a pouch of the entire pyloric antrum, were prepared so that the secretions from the fundic and pyloric mucous membranes could be collected simultaneously. These animals were used to demonstrate the reality of the gastrin theory because it was possible to apply substances to serve changes in the secretion of the Pavlov pouch. The method consisted in collecting two to three hours of continuous secretion (twenty-four hours after the last meal) from the Pavlov pouch and then in applying the various substances for a period of two hours to the mucosa of the pyloric pouch and at the same time continuing the collection of secretion from the Pavlov pouch. Application was made by injecting the substances into the pouch and then plugging the orifice with cotton, this being repeated every three to five minutes. In order to insure continuous contact a device was constructed (illustrated in the article) which prevented the pouch from expelling its contents. No increase in the secretion of the Pavlov pouch was obtained when such substances as strychnin sulphate, pilocarpin hydrochlorid, potassium iodid and food extracts were applied to the mucosa of the pouch.

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**Intestinal Saccharase.**

*E. Knaff-Lenz, Hoppe-Seyler's Ztschr. f. physiol. Chem., 119: 61, Berlin, March 14, 1922.*

That cane-sugar is inverted by the intestinal mucous membrane but not by pure intestinal juice is due to the behavior of intestinal invertin as an endo-enzyme, the same as yeast invertin; that is, its action takes place only at the cells' limiting layer, in this case Lieberkühn's glands, and does not enter the intestinal fluid. This conception is rendered doubtful histologically, as an actual secretion must be assumed in the case of goblet-cells, which form Lieberkühn's glands. To elucidate this question, experiments were carried out on surviving rabbit's intestine. Rabbits were bled from the carotid, the small intestine removed the content washed out, pieces of intestine of equal length filled with 10% cane-sugar solution and tied at both ends, suspended in Ringer's solution through which oxygen passed, and maintained at constant temperature in the water thermostat. After two hours the content was filtered, mixed with an equal volume 3% soda solution to interrupt inversion and prevent mutarotation, and the rotation of polarized light determined. The constants were calculated in the customary manner from the formula  $X=1 \div t (\log) R + L \div a + L$ . Three series showed that the surviving intestine is capable of inverting cane-sugar. The second and third experiments showed that a single irrigation of the intestine before the introduction of the sugar solution reduces the reaction velocity by one-half and two irrigations still more. Previously secreted invertin must therefore be present in the intestinal lumen. The negative results given by intestinal juice are due probably to rapid destruction of invertin by proteolytic ferment, and to the fact that cane-sugar constitutes the stimulus for the secretion of intestinal invertin.

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**Researches on Bile Acids. XI. The Oxidation of Cholic Acid.**

*Heinrich Wieland and Otto Schlichting, Hoppe-Seyler's Ztschr. f. physiol. Chem., 119: 76, Berlin, March 14, 1922.*

Letsche has dealt with the oxidative decomposition of cholic acid. By the action of nitrosulphuric acid he obtained an acid containing 5 fewer atoms,  $C_{19}H_{28}O_{10}$ . It is taken to be a pentabasic acid 3 of whose 4 cholic acid rings must have been opened as a hydrocarbon;  $C_{19}H_{38}$  is its foundation. Therefore the acid can contain only one ring. The oxidation of desoxycholic acid, carried out under the same conditions, at first opens one ring (desoxybiliaric acid,  $C_{24}H_{36}O_7$ ), further a second ring (choloidanic acid,  $C_{24}H_{36}O_{10}$ ) without reducing the hydrocarbon content of the molecule. The two secondary OH-groups of desoxycholic acid, on which oxidation begins, are in the same position in cholic acid. The difference in the result of oxidation must therefore depend on the third OH-group in the molecule of cholic acid. It was to be assumed that the opening of a third ring in cholic acid was due to its third OH-group. As these formulas were found to be different by other authors, biloidanic acid and derivatives of the same were prepared recently. Biloidanic acid was prepared by oxidation with nitric acid; yield 15%; disintegration point 228. It is obtained in fine crystals by allowing to crystallize from 60% acetic acid; specific rotation +11.28. The neutral methyl ester of biloidanic acid has a melting point of 91°-92°. The analysis and methoxyl determination permitted no decision between the two formulas,  $C_{19}H_{28}O_{10}$  and  $C_{24}H_{36}O_{12}$ . But, the molecular weight determinations undertaken in benzol, glacial acetic acid and naphthalin which lie sufficiently wide apart at 586 for  $C_{29}H_{46}O_{12}$  and at 486 for  $C_{24}H_{36}O_{10}$ , pointed unmistakably to the higher value. For further characterization, hydrochloric acid gas was led into the alcoholic solution of the acid and the triethylester,  $C_{29}H_{46}O_{12}$ , obtained by dissolving the same rapidly with dilute ammonia and precipitating with barium chlorid. The barium salt had a neutral reaction. The free ester, which was obtained by addition of hydrochloric acid, had a melting point of 200°-201°. Biloidanic acid trimethylester was prepared in the same way as the acid triethylester. Its melting point is about 213°. Trimethylester can be saponified to monomethylester like triethylester; its melting point is 223°-224°, its formula  $C_{19}H_{28}O_{10}$ . On boiling biloidanic acid a long time with water a splendidly crystallized hydrous acid is formed to which its discoverer gave the formula  $C_{19}H_{28}O_{10}+2H_2O$ . This acid melts at 145° with frothing and loss of water, then again solidifies and finally liquefies at 230°-231° with decomposition. The water of hydration of the acid is given off in vacuo after heating three hours at 115°. From cholic acid,  $C_{24}H_{40}O_5$ , the tribasic diketo-acid, biliaric acid,  $C_{24}H_{34}O_6$ , is formed; from desoxycholic acid,  $C_{24}H_{40}O_4$ , the tribasic monoketo-acid, desoxybiliaric acid,  $C_{24}H_{36}O_7$ . If desoxybiliaric acid be further oxidized with nitric acid, the second ring, which contains the CO-group, is opened in an analogous manner to the first ring.

Choloidanic acid has been recognized as a pentabasic acid,  $C_{24}H_{36}O_{10}$ . Regarding constitution it may be stated that biloidanic acid is isomeric with solanellie acid to which the authors penetrated, from desoxycholic acid with opening of the third ring. The two acids

show considerable differences. No satisfactory explanation for their different behavior under thermal decomposition is found, by which biloidanic acid loses two molecules  $\text{CO}_2$  (at  $230^\circ\text{-}240^\circ$ ), solanellic acid only one molecule. On the other hand norsolanellic acid,  $\text{C}_{22}\text{H}_{32}\text{O}_{12}$ , is very similar to biloidanic acid.

On boiling with water norsolanellic acid does not yield a hydrated acid, nor does it form, like biloidanic acid, any barium salt difficultly soluble on heating. If the deductions for biloidanic acid apply to cholic acid then one carbon atom more, namely 11, is free for the reception of the remaining molecule, the residual content  $\text{C}_{10}\text{H}_{18}\text{COOH}$ .

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### The Formation of Bile-Pigments in the Human Organism.

*S. J. Thannhauser, Klin. Wchnschr., 1:858, Berlin, April 22, 1922.*

The structure of blood-pigments must be studied in order to determine the origin of bilirubin from the blood-pigment. Hemin contains iron and chlorin. The chlorin is not preformed in the blood-pigment, but is combined as a salt with the iron which is attached to the nitrogen of the 4 preformed pyrrol rings of the hemin.  $\text{O}_4$  in the hemin molecule represent 2 carboxyl groups. The reduction might take place in the vinyl groups of the side chains, which are converted into ethyl groups; the substance formed in this way is called mesohemin. In complete reduction, the hemochromogen cannot be prepared because of its extraordinary sensitiveness to oxygen. The iron-free porphyrins are formed from hemin. The 2 carboxyl groups are still found in the porphyrins, because of which they have basic (forming complex salts) and acid characteristics (forming esters). The 2 vinyl groups of the side chains in the mesoporphyrin are saturated into ethyl groups by taking up hydrogen. The fundamental substance of the porphyrins, containing no oxygen, is the ethioporphyrin, which Willstätter obtained from the prophyrrins of chlorophylls, by which he established the similarity in the structural formation of blood-pigments and leaf pigments. The leuko-compound of the porphyrins (porphyrinogen) contains no iron, corresponds to hemochromogen, and, has not the capacity to form iron compounds. A mixture of pyrrol bases (hemapyrrol, phyllopyrrol, cryptopyrrol and methylethylpyrrol) and also an acid fraction from the corresponding carbonic acids, results from reduction of the hemin molecule. Bilirubin is in close but complicated relation to the iron-free porphyrins, but is differentiated from the latter by the fact that it does not form complex salts with iron, and the imido nitrogen of the pre-formed pyrrol molecule give a different reaction. Mesobilirubin is obtained by reduction of bilirubin which bears the same relation to bilirubin as mesohemin to hemin. The preformed vinyl groups in the hemin are also present in bilirubin.

Mesobilirubin can be converted into its leuko-compound (mesobilirubinogen) which is identical with urobilinogen. Hematinic acid results from oxidation of bilirubin, the reduction of this acid differs radically from the reduction of blood-pigment. The analogy between the two pigments is evident from the molecular weight and the chemical characteristics. The structural frame of both is 4 pyrrol rings, in which 2 unsaturated vinyl groups and 2 carbonic acids are attached to  
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the side chains. The presence of hydroxyl groups in 2 pyrrol rings of the bilirubin frame is probably the important difference between the porphyrins of the blood-pigment and the bile-pigment. The iron-containing pigment "hemosiderin" cannot be looked upon as a unique chemical substance; at any rate it is not a connecting link between blood-pigment and bile-pigment. It is not known where the complex formation of bile-pigment from hemoglobin occurs. Varying views are held regarding the identity of hemotoidin and bilirubin, which forms the basis for the theory of extrahepatic bilirubin formation. The occurrence of icterus, the abnormal accumulation of bile-pigment in the biliary capillaries and blood serum is intimately related to the point of origin of the biliary pigment. Bilirubin and urobilinogen are the normal metabolic products of the decomposition of blood-pigment; it has not been explained as yet to what degree they may serve after resorption for renewal of blood-pigment.

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#### The Rôle of the Liver in Intermediate Metabolism.

*Fritz Laquer, Klin. Wchnschr., 1: 822, Berlin, April 22, 1922.*

The chemical changes in intermediate metabolism probably take place mostly in the liver. Decreased function of the organ and the appearance of pathologic products in severe disease of the liver permit conclusions as to the normal liver function. The liver is involved in the most important metabolic diseases, diabetes, acidosis, alkapttonuria and gout. Experiments on the surviving organ are valuable, in spite of many objections, and offer much information as to liver metabolism.

In the internal metabolism of the liver, the consumption of oxygen increases 10 fold during digestion. Freise showed that carbohydrate can be consumed in the perfused liver. Liver pulp can change salicylic aldehyd into salicylic acid, not by oxidation, but by reduction of oxid. Hofmeister believes it probable that all of these functions of the liver are inherent in the individual liver cell.

Under intermediate metabolism the author includes such endothermic and exothermic processes which cannot be determined to take place exclusively in the liver. The sugar metabolism of the liver is best understood. The liver has both a glycogenic and sugar-hoarding function. The sugar is stored in the form of glycogen and the liver can form glycogen from the most varied monosaccarids. There is a difference in the functional ability of the intact liver and the organic pulp, for instance in the transformation of fructose into dextrose, the activity of the necessary stereokinases appears to be related to the cellular structure. The glycogen deposits of the liver are depleted during severe muscular work and hunger. The conversion of glycogen to dextrose is a "purely fermentative" process, not inherent in the cell structures. The metabolic interchange with the rest of the body is regulated by the nervous system and hormones; the vagus represents the centripetal, the sympathetic system the centrifugal paths of these reflexes. The mode of action of the endocrine glands is not exactly known; and it is also unknown whether the hormone action is limited to the liver or also includes the muscles. Adrenalin causes increased sugar outflow, but only with intact liver structure. Changes of the hydrogen-ion concen-

tration of the blood influence the ferment process involved in the conversion in sugar; since acids are formed during muscular activity, there is a simple regulation of the outflow of sugar by the sugar utilization. The heat of combustion in the lactic acid of the dextrose is utilized by the body for reconversion of sugar. The trioses dioxy-acetone and glycerin aldehyd are intermediate products, which form hexoses in the perfused liver, and sorbose from glycerin aldehyd.

The liver also serves as a store-house in fat metabolism; in experimental phosphorus poisoning fatty liver is caused by infiltration, the fat is not formed here but originates from without, but it may be admitted that the liver has the capacity of forming fatty acids from shorter carbon chains. Acetone bodies are derived from numerous amino-acids, which normally are decomposed in the liver. Probably aceto-acetic acid decomposes into 2 molecules of acetic acid by addition of water; the fate of this is not definitely known, most of it is surely consumed, with intermediate formation of oxalic acid, perhaps also glycolic acid, glyoxalic acid and formic acid, perhaps by reduction of the acetic acetaldehyd.

Lastly, albumin is stored in the liver, though in small quantities. The decomposition of albumin produces the corresponding amino-acids; these are deaminized by oxidation, and the resulting ammonia serves for urea synthesis. The liver probably transforms certain poisonous interstitial products of protein digestion into noninjurious form. The relations between carbohydrate metabolism, fat metabolism and protein metabolism in the liver are of special interest. Urea is formed not only through splitting up of arginin, but the relation of other factors has not been determined owing to the complexities of the intermediate purin metabolism.

Among "pairings" in the liver, that of carbolic and cresol with sulphuric acid represents the most important. A number of foreign substances are excreted in the urine in combination with glycuronic acid; this synthesis also probably occurs in the liver. The pairing of benzoic acid and glycocoll into hippuric acid probably occurs not only in the kidneys but also in the liver. The physiology of the liver serves as an example of the value of a close relation between the clinical and purely theoretic research.

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#### The Influence of Chlorophyl Preparations on Human Metabolism.

*Harry Koenisfeld, Ztschr. f. d. ges. exper. Med., 26: 216, Berlin, March 6, 1922.*

In the course of former researches the author was able to show that the chemically most active ultraviolet light rays exert a considerable influence on total human metabolism, especially on nitrogen metabolism, in the sense of an increase. Experimental results do not as yet permit of a well-founded theoretical explanation of these phenomena in which photocatalytic processes may be involved. From the side of physiology emphasis is laid on the increase of metabolism under the influence of light, though no absolutely certain data are as yet available. In pursuance of these conceptions it seemed of interest to determine whether biochemical processes that proceed more rapidly under the influence

of light than of darkness are affected when substances which show a special reaction to light are supplied to the organism. Such substances are represented particularly by fluorescent bodies. For practical reasons the author investigated the influence of chlorophyl on human metabolism. After a five days' preliminary test the 3 experimental individuals received 3+3 iron-free chlorosan tablets (a preparation containing chlorophyl), followed by a five day period with the same regimen. The diet consisted of previously prepared food, namely potatoes and butter fat. Nitrogen was estimated by Kjeldahl's and sodium by Volhard's method, while the estimation of sulphuric anhydrid was effected by titration with barium chlorid, that of phosphoric anhydrid with uranium acetate. In all cases an increase in eliminated nitrogen and phosphoric anhydrid, and on one occasion of sulphuric anhydrid, was found. The increase in nitrogen elimination takes place through the stools and not through the urine. Hence the chlorophyl preparation increases nitrogen metabolism.

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### The Pharmacology of Cellular Respiration.

*Philipp Ellinger, Hoppe-Seyler's Ztschr. f. physiol. Chem., 119: 11, Berlin, March 14, 1922.*

The elucidation of the physiologic mechanism of cellular respiration was facilitated by the finding of 2 different groups of substances (hydrocyanic acid and narcotics), that arrest oxidation. Substances increasing oxygen consumption of blood-corpuscles are pnein, (obtained from different body tissues by Batelli and Stern), the various respiratory bodies prepared by Meyerhof from yeast juice and from the juice of various animal tissues, and finally the cellular substrate obtained by Ellinger by freezing goose erythrocytes. Cellular oxidation was demonstrated by Warburg in models, and the combustion of amino-acids on animal charcoal. But, as the lyophobe charcoal behaves differently to the lyophil components of cellular structures, cell debris suspensions obtained by destruction of erythrocytes by freezing and subsequent washing of the cellular substrate with Ringer's solution were also employed. Oxygen consumption was determined with Barcroft's manometers. The content of the vessels up to the meniscus of the intercepting liquid amounted to 18.7 c.c.; carbonic acid was intercepted in each case by 0.3 c.c. normal lye; the liquid to be tested was always 2 c.c., the reaction temperature 39.8° and the oxidations took place in air. For 1 mm. pressure decrease of Brodie's liquid an oxygen consumption of 1.432 cu.mm. was obtained. Controls were carried out in all experiments. In all cases goose erythrocyte suspensions, animal charcoal suspension and suspensions of washed goose erythrocyte cell debris were examined for oxygen consumption. Experiments were conducted to determine the oxidation rate with varying concentrations of cell debris. Oxidation rate was highest in the highest concentration, three-fourths of the final value being attained after one hour and the total value after two hours. With decreasing concentration the oxidation rate decreased constantly but considerably. The material employed for the tissue components of endocrine glands consisted of dried organic powders of the thyroid, ovary, testicle, mamma, thymus, cerebrum,

hypophysis, suprarenal gland and liver. The preparations were soaked in Ringer's solution and then sterilized. Further, a number of optones was studied; these were obtained from the respective organs (thyroid, ovaries, testicles) by a fermentative decomposition process. In all cases the action of these bodies in 1% solution showed increased oxygen consumption, which was arrested after a while. The percentage increase in respiration differed in erythrocyte suspensions of different oxidation rates. On the other hand, the absolute increase of oxygen consumption was found to be the same with blood-corpuscle suspensions of different origin and proportionate to the amounts of the substances supplied. The highest values were generally yielded by optones, while no material differences existed between untreated glandular preparations and pepsin-digested products. Later experiments showed that 2 types of substances increase oxygen consumption by goose erythrocytes in different ways. There are bodies that increase the nutrient material, and there are others which, though not furnishing new nutrient material, alter the sites at which oxidation takes place and thereby induce a more rapid oxidation of the combustible material. The tissue components of endocrine glands do not contain any substances that can be regarded as hormones of erythrocyte species. They all contain oxidizable bodies, probably amino-acids, that serve as combustible material, but do not represent a specific character of endocrine glands. Experiments on gelatin and protein cleavage products show that albuminoids which in themselves exercise no influence on the species may be converted by solution into substances that increase the oxidation rate by supplying new nutrient solution. Nonrespiratory cell debris emulsion offers a model of respiration which represents a closer approach to the actual conditions than the animal charcoal, inasmuch as the influence on respiration of intumescent and superficially active substances may be observed. Urea increases the oxidation rate in goose erythrocytes by enlarging the adsorption surface without itself being oxidized. On the other hand quinin diminishes erythrocyte respiration by reducing the adsorption surface. Sodium salicylate does not affect the oxidation rate. The reduction of the oxidation rate by means of radio-active alpha rays must be regarded as a mechanical destruction of the cellular structure. The increase in the oxidation rate due to increased potassium content of the nutrient solution must also be assumed to result from surface alteration.

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The Relations between Fertility and Nutrition. II. The Ovulation Rhythm in the Rat on Inadequate Nutritional Régimes.

Herbert M. Evans and Katherine Scott Bishop, *J. Metab. Research*, 1: 335, March, 1922.

General results of experiments conducted on several hundred individuals during the past two years are summarized.

(1) *The Effect of undernutrition with a balanced diet on attainment of sexual maturity and on ovulation rhythm*:—It had been shown previously that the diet employed, when administered in sufficient quantities, constituted an adequate nutritional régime in the rat for growth and reproductive performance. Consumption of this diet was limited to create partial starvation and stunting. Three different nutritional

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levels were maintained resulting in 3 corresponding weight levels. The rats and controls were observed 375 days with daily microscopic examination of vaginal smear to determine occurrence of oestrus and ovulation. The experiments showed that the time of maturity, the ovulation rhythm and the degree of suppression of the oestrus vary according to the degree of starvation.

(2.) *Effect of changes in the proportion of carbohydrate, fat and protein.*—Although the rat grows well on a diet almost entirely lacking in fat or preformed carbohydrates; the maintenance of ovulation rhythm and reproductive capacity constitute a more exacting test of sound physiology than growth alone. The test was applied to animals reared on fat-low diets and preformed carbohydrate-free diets. In both groups vitamin requirements were satisfied by feeding separately daily 0.4 gm. dried whole yeast and either 0.2 gm. dried alfalfa leaves or, in the lard diets, 5% butterfat content. Results show that the growth of animals fed on carbohydrate-free diets in which protein was medium in amount, was approximately normal, nor was there significant injury to sex physiology, maturity was not delayed and the proportion of short oestrus cycles not much decreased compared to controls. But with very low protein (12%), great stunting, delayed maturity and fewer oestrus periods resulted. The withdrawal of fat acted injuriously on the sex organs, this being least with a protein content of 23% or 50%. With low protein (12%) it is remarkable that normal growth occurred though the function of sex glands was depressed, maturity delayed and ovulation less frequent.

(3) *Undernutrition due to qualitative deficiency of the protein.*—The inadequacy of wheat protein, when this grain is used as the sole source of protein, was shown. McCollum's diet was used. Adults placed on this diet 100-200 days were not injured but young animals reared on it were badly stunted and oestrus periods and ovulation much affected. Addition of casein to this diet effected restoration.

(4) *Effect of deficiency of salts.*—Salt-deficient diets have a definite effect on oestrus. Sex impairment is much in excess of growth impairment. Salt-deficiency is inimical, not only to skeletal growth, but also to normal ovulation rhythm for unknown reasons.

(5) *Disturbance due to reduction of fat-soluble vitamin A.*—Adult rats that had previously received adequate diet, when placed on low vitamin A diets for long periods, showed no injury, but with greater vitamin-deficiency, disturbance of ovulation rhythm took place. The disturbance of oestrus from fat-soluble vitamin A deficiency is highly characteristic.

It consists in the prolongation of the oestrus desquamative changes in the vaginal epithelium throughout the entire period of acute deficiency. It may constitute the only symptom of vitamin lack save failure to reproduce successfully. That the body stores, and utilizes stored, vitamin A is convincingly shown by this new test.

(6). *Disturbance due to reduction in supply of water-soluble vitamin B:*—Ovulation is more sensitive to this deficiency than is general bodily nutrition; oestrus is not prolonged as with vitamin A deficiency but is obliterated.

(7). *Disturbance of ovulation rhythm on diets consisting of single natural foodstuffs:*—The prevalent opinion that rats fail entirely on

a purely carnivorous diet is not confirmed. On a purely milk diet their sex physiology is rendered abnormal though growth is not greatly depressed.

(8). *Disturbance of ovulation rhythm on supposedly adequate diets*:—The results of the study of ovulation compel the recognition of more sensitive tests of well-being than that furnished by the growth rate. Animals that grow normally may be so seriously impaired in their reproductive organs as to depart widely from the normal ovulation rate.

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**A Study of Weight Regulation in the Adult Human Body during Overnutrition.**

*Addison Gulick, Am. J. Physiol., 60: 371, April 1, 1922.*

The purpose of the experiments here reported was to establish constancy of weight at various levels of total intake. In order to insure the adequacy of the protein and accessories throughout the experiment, milk and eggs figured in all the dietaries. Small amounts of fats were used but excesses were avoided because of the possibility that fats might be shunted into the adipose tissue, making a passive increase of body weight without in any way having shared in the metabolism. The main source of nourishment was carbohydrate, from rice, wheat and oats, and the experiment consisted chiefly in varying the quantity of starchy food from these sources. The first test in March, April, and May, 1916, was to find the minimum diet that would maintain an approximately normal body weight. After that the purpose was to establish a constant weight on a high level of exchange. This attempt lasted with interruptions from May, 1916, to July, 1917. At the height of this period of maximum weight and food intake the basal metabolism was determined by the analysis of gas exchange. The body weight was then brought back rather abruptly to the initial level by means of a low calorie diet in July and August, 1917. To conclude the experiment, another determination was made of the quantity of food necessary to hold the weight constant. The general results of the experiments were that the subject (a person belonging to the difficultly fattening type) was found to show a wasteful rate of oxidation during all the feeding experiments, including both the periods in which the diet was moderate or low and those in which a large excess of starch was superposed upon the normal diet. During the prolonged periods of high diet this wasteful oxidation became more pronounced, and it continued so throughout the following periods of undernutrition, so that even after the body had been brought down again to its original weight, it required more food to keep it at steady weight than had been necessary at the start. Gulick found that the subject owed his resistance against fattening to an extravagant calorie requirement which persisted at all times, despite a moderate daily round of activities. This extravagance increased during the course of the excessive carbohydrate diet, and stayed above the initial level even after the return to normal weight. The basal metabolic rate was not involved, but remained strictly normal.

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**Experimental Researches on the Absorption of Fat in the Stomach.**

*Sozo Hirayama, Japan Med. World, 2: 101, Tokio, April 15, 1922.*

A series of experiments were conducted on various genera of animals to determine whether or not fat is absorbed in the stomach. Several hours after the feeding of fat, there was a gradual increase of fat in the epithelium of the gastric mucosa and a gradual penetration toward the deep layer, reaching finally the zenith of fat-content which was followed by a gradual decrease to normal, showing that the epithelium of the stomach can absorb fat. The following facts disprove the theory that the fat globules are not absorbed in the stomach, but are absorbed in and excreted by the intestinal canal. (1) The fat increase begins in the upper epithelium and gradually penetrates the deep tissue; if the fat globules were excreted from the stomach, the increase of fat in each successive layer as time passes would be in an inverse proportion. (2) Even after the amount of fat of the gastric mucosa returns to normal, the fat absorption still continues actively in the intestine.

The gastric mucosa absorbs fat throughout the life of mammalian and cold-blooded animals, but in the latter the absorption decreases with growth. The absorptive power varies in different animals and in different portions of the same stomach: in mammals absorption is most active at the pylorus and in cold-blooded animals at the fundus. In cold-blooded animals the absorption occurs later than in mammals. The gland cells show less absorption than the epithelium. Fat globules are absorbed more quickly than neutral fat. The cat is the most suitable animal for this test.

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**Fats and Carbohydrates in the Dietary.**

*Sabato Visco, Riv. di biol., 4: 1, Rome, Jan.-Feb., 1922.*

A diet composed exclusively of proteins is not long tolerated, especially by individuals at rest; on such a diet the nitrogen equilibrium is maintained only by high amounts and for an indefinite period of time. If, however, to such a protein dietary be added substances of the other two classes of foodstuffs, all nutritional disturbances disappear; there is a diminution in the amount of protein necessary to restore the nitrogen balance, and toxic symptoms no longer occur. The author has attempted to determine which of these two groups of foodstuffs best accomplishes this effect, whether it is more advantageous to add carbohydrates or fats to the protein ration, or whether, from a physiologic standpoint, it is immaterial which of these is added.

Experiments were carried out on adult rats, apparently in the best state of health and nutrition. To the various test food mixtures there were added 2% of cow's milk ash, in order to avoid demineralization.

The results seem to indicate that absorption of nitrogenous foods is more readily accomplished when they are administered with fats than when given in combination with carbohydrates. The ratio of nitrogen excreted in the urine to the nitrogen ingested in the food is always higher when the diet consists of a mixture of proteins and fats than

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when a mixture of proteins and starch is taken. Rats fed on mixtures of proteins and fats in the proportion of 1: $\frac{1}{3}$ , 1:1, and 1:2 constantly increased in weight. Rats fed on protein and carbohydrate mixtures (the latter in the form of soluble starch) in proportions of 1:1, 1:2, and 1:4 constantly lost weight.

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**The Destruction of Lactic Acid by Yeast and Blood-Corpuscles.**

*Otto Fuerth and Fritz Lieben, Biochem. Ztschr., 128:144, Berlin, March 7, 1922.*

The authors endeavored to determine more accurately the conditions under which lactic acid is destroyed by isolated cells (yeast and erythrocytes). For the estimation of lactic acid the aldehyd method was employed, (oxidation of lactic acid in hot sulphuric acid solution by addition of permanganate in drops and iodometric estimation of the aldehyd distillate with added bisulphite). In order to avoid the losses occurring in the aldehyd method the results were multiplied by the routine factor 0.005. A source of error in Ohlsson's extraction method for lactic acid was obviated by driving off amyl alcohol with steam. The experiments show that yeast, as well as bloodcells, are capable of rapidly destroying large amounts of lactic acid by oxidation under suitable conditions. In the destruction of lactic acid by these two agents, however, neither the optical activity of lactic acid, nor the temperature, nor oxygen pressure, nor the presence of a hydrogen acceptor (methylene-blue) is of determining importance. The important factor is the intimate contact of constantly renewed oxygen with the cell body. The destructive action is arrested immediately (or may become regressive) when the gas exchange is arrested, as in the closed gas bomb. The conduction of oxygen through an open vessel, in which the yeast suspension is kept agitated so that the yeast cells not merely come in constant contact with new oxygen particles but give off their metabolic products, caused the disappearance of lactic acid except slight traces. The amounts of lactic acid destroyed in the course of six to fourteen hours varied from 0.2-0.3 gm. in experiments employing 25-50 gm. press yeast in aqueous suspension. The disappearance of lactic acid from the yeast suspensions was attended by the evolution of considerable amounts of carbon dioxid, which could be only partly explained by the simultaneous disappearance of sugar from the alcoholic fermentation (or by boiling hydrolyzable carbohydrate with hydrochloric acid 2.2%). The major amount of lactic acid is not oxidized completely to carbon dioxid and water, nor is it reconverted into sugar. There were no indications of an accumulation of considerable amounts of volatile acids or substances that form iodoform, of methyl glyoxyl, alcohol, acetaldehyd, pyroracemic acid, acetone or aceto-acetic acid in the yeast mixtures after the disappearance of the added lactic acid. The capacity of yeast for destroying lactic acid is materially affected by abolition of its living activity, by the action of acetone, or by boiling temperature. According to Slosse the decomposition of sugar in the blood occurs from glucose to lactic acid + lactic acid, to acetic acid + formic acid, to carbon monoxid. Regarding the fate of the disappearing lactic acid it is probable that even more favorable conditions are offered by

the use of animal cells. The capacity for forming lactic acid from sugar and the ability to decompose lactic acid by oxidation are apparently a common property of living cells.

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**Carbohydrate Catabolism in the Animal Body.**

*Gustav Embden, Klin. Wchnschr., 1:401, Berlin, Feb. 25, 1922.*

This work discusses chiefly the intravital changes in the carbohydrate molecule. Taking the carbohydrates and their intermediate products as an example, there is no absolutely exclusive form of metabolism for any certain class of nutritive materials. The reversible reactions in intermediate carbohydrate metabolism are of great importance. In considering the chemical processes involved in the catabolism of the dextrose molecule which ends in the formation of carbonic acid and water, 2 principal phases are distinguished: (1) splitting of the molecule without taking up oxygen; (2) oxidation of the cleavage products. Lactic acid, long known as a product of intermediate metabolism, is produced in the catabolism of carbohydrates. From the chemical formula, Embden explains his belief that a molecule of dextrose breaks up into 2 molecules of glycerin aldehyd. Glycerin aldehyd appears as an intermediate product in the conversion of dextrose into lactic acid, and is, moreover, much more readily transformed into lactic acid than is dextrose. Of the 2 optically isomeric lactic acids, only the dextrorotatory form appears in the animal organism. When glycerin aldehyd is used a mixture of d-e lactic acids is produced, the latter predominating, which, however, does not contradict the assumption that glycerin aldehyd is an intermediate product, for considering the optical nature of glycerin aldehyd, racemic aldehyd would necessarily give rise to both forms of lactic acid. Experimental perfusion of the liver and experiments with fresh pulp of organs have shown that glycerin is formed from glycerin aldehyd and from the corresponding ketose, dioxyacetone, and, on the other hand, in the liver poor in glycogen, glycerin is readily transformed into d-lactic acid and under favorable conditions into glucose. Both processes doubtless occur through the intermediate formation of triose. Even though the formation of glycerin, so far as it relates to carbohydrate metabolism is only a by-effect, it is biologically important and possibly the only way for the conversion of carbohydrates to a characteristic constituent of neutral fat.

Isaac attributed death from phosphorus intoxication to the loss of the liver's capacity for forming sugar by synthesis from lactic acid. In the oxidative phase it is evident that the secondary alcohol is first transformed into the corresponding ketonic acid. This is indicated by the capacity of milk and pyroracemic acid to be transformed into d-alanin, and also by the transformation of amino-acids into oxy-acids by oxidative deaminization through intermediate formation of ketonic acids. The reduction of pyroracemic acid to d-lactic acid is a reversible process as is the reduction of beta-oxybutyric acid to acetic acid. This further conversion of pyroracemic acid is through acetaldehyd, acetic acid, beta-oxybutyric acid, and this indicates the first step in conversion of the carbohydrates into the lower and then higher fatty acids. The reversibility of the process extends to the oxidative phase. The

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carbonyl groups contained in 3 of the intermediate products are of importance as they give rise to biologically important reactions. A study of the relations of the phosphoric acids to animal carbohydrate metabolism is under way.

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**Stimulating Effect of Nutrition on Purin Metabolism.**

*Ernst Joel, Klin. Wchnschr., 1:735, Berlin, April 8, 1922.*

If food is taken that contains large amounts of nucleic acid or purin bases, only a fraction of the uric acid represented by the amount of purin taken appears in the urine; but if sufficiently small amounts of meat are taken, not only is the entire amount of uric acid contained in the purin excreted, but a considerable excess is also excreted within a few hours. Uric acid can therefore not be regarded as a direct derivative of the nucleus of the food; it is probable that the purins of the food act rather as mobilizing stimuli. This is indicated by the fact that repeated stimuli have a progressively weaker action and that the organism tries to compensate for an excessive action by a later decrease in uric acid excretion. A considerable excretion of uric acid, caused by the administration of atophan, rendered an otherwise extremely active thymus meal ineffective, as its nucleins were utilized for substitution in the body.

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**The Retention and Distribution of Amino-Acids with Especial Reference to the Urea Formation.**

*Otto Folin and Hilding Berglund, J. Biol. Chem., 51:395, April, 1922.*

The authors made a critical and experimental examination of the hypothesis that deamination and urea formation are localized in the liver. Since all observers are now agreed that the greater part of the protein is absorbed as simple amino-acids and that the amino-acids, which pass the liver are absorbed by all the other tissues, the whole problem has narrowed down to the one question of whether the absorbed nitrogen does or does not pass out of the liver in the form of urea. Table I gives the identical results obtained in 2 subjects who took a substantial meal, without any preceding breakfast, at 11:45 a.m. to 12 m. The meal consisted of 3 boiled eggs, 1 pt. milk, bread, butter and coffee. The figures show that within one and one half hours the amino-acid content of the plasma rose from 5.2 to 5.8 mg. per 100 c.c. In the course of the next hour it rose to 6.4 mg., and five and one-half hours after the ingestion it had again sunk to very near the fasting value. The experiment was made principally to show that an ordinary meal not excessively rich in protein, is accompanied by a slowly increasing concentration of the amino-acids in the blood, an important fact since it is known that accompanying that increase there must be a large increase in the amino-acid content of the muscles. The amino-acid determinations were made by the new colorimetric methods previously described. The amino-acid excretion with the urine confirmed the values obtained for the blood. Table II gives the figures for blood and urine after a subject took 135 gm. gelatin dissolved in 900 c.c.

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water. In this case the amino-acid content of the plasma increased 100% in two hours (rising from 5.5 to 11 mg.), accompanied by a slight diminution in the urea content of the blood. The urea formation begins to gather force only after the incoming tide of the amino-acids has begun to subside. During the first two hours, while the amino-acid nitrogen rose from 5.5 to 11 mg., the urea nitrogen sank from 17.3 to 14.2 mg. Then during the next hour and a quarter, while the amino-acid nitrogen sank to 7.2 mg., the urea nitrogen rose from 14.2 to 20.2 mg. These fluctuations are believed to prove that the liver has no specialized function in connection with deamination and subsequent urea formation. The figures for the urea nitrogen or the total nitrogen of the urine tell the same story as the figures for the blood. Concerning amino-acid excretion as a test for nonexistent liver function the authors remark that it has no justification, although in suitable modified form it may have some value.

In studying the significance of the normal excretion of amino-acids it seemed possible that the amino-acids of normal urine, like the carbohydrates of the same, might for the most part represent denatured or more or less foreign nitrogenous materials, rather than the ordinary amino-acids which are the main constituents of food proteins. However, the increased amino-acid excretion obtained from the ingestion of 25 gm. glycocoll showed that the amino-acids found in urine represent losses of ordinary usable amino-acids. To study the question further a subject was given casein as well as creatin. Casein was chosen because it is a protein in which there should be no unusable nitrogenous materials. Results demonstrate that losses of ordinary usable amino-acids occur normally and are increased during and immediately following increases in the amino-acid content of the blood. In Table VIII are given data showing the effect of carbohydrate intake on the composition of blood and urine. At noon 200 gm. pure glucose in 830 c.c. water were ingested, immediately after taking a sample of the subject's blood. Small but definite reductions in the different nitrogenous constituents in the blood followed, due to the absence of nitrogen intake and the protein-sparing action of the sugar.

Concerning Falta's assertion that the blood-corpuscles are free from nonprotein nitrogenous constituents, the authors believe their analyses of plasma and whole blood reported in this paper prove that human blood-corpuscles are as permeable for nitrogenous constituents as they have previously been shown to be for glucose.

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#### The Influence of Meat upon Physical Efficiency.

*S. H. Bassett, Evelyn Holt and F. O. Santos, Am. J. Physiol., 60: 574, May 1, 1922.*

Experiments covered 4 different periods of one week each in length. During the first week the usual normal diet was taken by each subject. During the second week a luncheon containing 300 gm. beef was served, together with bread, butter and boiled potatoes, in the laboratory. During the third week little or no meat was taken, and during the fourth week the same procedure as in the second week. The 4 subjects analyzed their urine daily for nitrogen; all wore pedo-

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meters for measuring their daily movements. The tabulated results show that the presence or absence of meat from the dietary, during periods as long as one week, has no demonstrable effect upon the capacity for an amount of work so graded as to reach the limit of physical endurance for a short period of time. Removal of meat from the dietary for a period of one week did not diminish the sense of well-being in the individuals investigated.

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**Studies on Alkalogenesis in Tissues. I. Ammonia Production in the Nerve Fiber during Excitation.**

*Shiro Tashiro, Am. J. Physiol., 60: 519, May 1, 1922.*

From preliminary experiments the author made the tentative assumption that besides carbon dioxid there is at least one other volatile compound produced when a nerve is stimulated. This paper discusses in detail the possible chemical nature of this other volatile compound, giving each step in the experimental procedure, which leads Tashiro to believe the substance is an amin or ammonia. The fact that this compound is volatile and forms a yellow complex salt with Nessler's reagent and a white precipitate with Graves' reagent, strongly suggests that it is ammonia gas, but does not absolutely rule out the possibility of its being one of the volatile amins. By estimating the basicity produced by this compound, one may calculate it on the basis of ammonia and compare the results with those obtained by Nessler's or Graves' methods using standard ammonium salt. If such results do not agree with each other, one may calculate the basicity on the basis of all volatile amins, and compare the results obtained from the other method using standard solution of various alkyl ammonium salts. By means of the method described ammonia can be measured in quantities as small as 0.000,000,1 gm.

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**The Rôle of Vitamins in Cell Chemism. Supplement to the Communication of W. R. Hess.**

*Emil Abderhalden, Hoppe-Seyler's Ztschr. f. physiol. Chem., 119: 117, Berlin, March 14, 1922.*

The influence of the so-called vitamins on the total gaseous exchange has already been determined by Abderhalden and his co-workers. Hess employed dye methods in studying the oxidizing capacity of the tissues. Abderhalden considers the direct gaseous exchange experiments less ambiguous and refers to the entire chain of observations: On the one hand, temperature reduction (objectively determinable with the thermometer, observable further on touching the animals and by ruffled plumage; if several animals are in the cage they congregate close together); restricted total gaseous metabolism and diminished gaseous exchange in the different tissues. On the other hand, rising body temperature after intake of substances derived from yeast or bran, increased total gaseous metabolism and increased tissue gaseous exchange, point to severe affection of the oxidizing processes in the cells with one-sided nutrition of pigeons and other animals of similar be-

havior. The author has brought the peculiar spasmodic symptoms (disturbance of consciousness, drowsiness of the experimental animals) in short the disturbances depending on the nervous system, into relationship with the sensitiveness of nervous organs to oxygen deficiency. Whether the absence of definite substances influences, directly or indirectly, the oxidizing processes in the cells, remains to be determined. Researches are proceeding to determine whether the influence of those substances on the symptoms of hydrocyanic acid poisoning, temperature reduction, diminished gaseous exchange and alimentary dystrophy in rice pigeons can be determined.

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**The Relation of Photosynthesis to the Production of Vitamin A in Plants.**

*J. Walter Wilson, J. Biol. Chem., 51: 455, April, 1922.*

Since the green parts of plants appear to be among the richest sources of vitamin A, while seeds, in general, contain only traces of it, it seems apparent that the plant must synthesize the vitamin A found so abundantly in its leaves. To determine whether the production of vitamin A is dependent upon photosynthesis, wheat seeds were sprouted in wooden trays on moist paper, one lot in the dark room and another in the sunlight. When the sprouts were from 2 to 3 in. high, they were cut off close to the seeds, dried in a current of air at about 60° C. and ground into fine powders. These were fed to young white rats in a diet deficient in vitamin A, 5% of the powdered sprouts taking the place of an equivalent weight of cornstarch. The resulting growth curves show that either etiolated or green wheat sprouts furnish an adequate amount of vitamin A when the dried sprouts make up 5% of the diet of white rats. Since this proportion of sprouts represents a quantity of seeds which, if included in the diet, would be inadequate as a source of this vitamin, the conclusion is drawn that vitamin A is produced in the growing plant with or without any accompanying photosynthesis.

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**The Comparative Antiscorbutic Values of Milk.**

*J. M. Johnson and C. W. Hooper, Pub. Health Rep. (U.S.P.H.S.) 37: 989, April 28, 1922.*

A comparative study of a variety of milk and milk powders in relation to their antiscorbutic value was undertaken. Guinea-pigs were kept in individual cages and fed hay and oats ad libitum and given milk of a definite variety instead of water. The animals were examined 3 times weekly for symptoms of scurvy. The findings indicated that no positive diagnosis of scurvy can be made without histologic examination of the costochondral junctions, yet much of the research on scurvy can be made without histologic examination of the costochondral junctions, yet much of the research on scurvy in guinea-pigs has been published without such histologic data. The 8 varieties of milk included fresh raw milk from a farm of the U. S. Department of Agriculture, certified milk not over twenty-four hours old, milk pasteurized at 145°F., reconstructed milk made from milk powdered by the spray

process and fresh butter, and 4 forms made from milk powder prepared by the spray process and the roller process. Forced feeding was not resorted to. The results of the tests indicate that the raw milk from the Department of Agriculture dairy and milk made from the roller process powder especially prepared for infants gave the best results in point of growth and absence of scurvy. The results in general indicated that drying and pasteurization have a destructive effect on the antiscorbutic vitamin. Certified milk is not far superior to reconstructed and pasteurized milk and, in fact, did not seem to give as good results as the roller process dried milk. It would appear, however, that no milk will certainly prevent scurvy unless the animal is forced to consume large amounts daily.

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**Experimental Studies with Proprietary Vitamin Products.**

*Julius H. Hess, Josiah J. Moore and Joseph K. Calvin, J.A.M.A., 78:1441, May 13, 1922.*

The first product studied was one known by the trade name of Metagen. It was shown by experiments on guinea-pigs that Metagen as obtained in the open market contains no demonstrable amount of antiscorbutic substances. The effect of the aging of this product after leaving the manufacturing laboratory may be of importance. The second product was known commercially as Vitamon. Animals fed a scurvy-producing diet, plus Vitamon, without exception developed scurvy in from fourteen to sixteen days. A third product, now in the process of experimental preparation, which contained orange juice and desiccated pig's liver, was investigated at the manufacturer's request. All the animals fed on the larger doses of this product died, it being the impression that this was due to the toxic effect of the product, the use of which was started two weeks after its receipt from the manufacturer.

Experiments on pigeons were made with the concentrated preparations for their antineuritic potency. It was shown that the process of manufacture and subsequent aging of the concentrated vitamin products had not caused as much deterioration of the antineuritic as of the antiscorbutic properties. The products had a much lower potency than fresh yeast, with the possible exception of the Yeast Vitamine-Harris preparation. The claims that one or all of the known vitamins can be prepared for dispensing in a concentrated form are open to question. The best method of obtaining sufficient vitamins is through a proper selection of foods.

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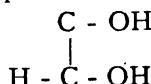
**Permeability of the Glomerular Membrane to Stereo-Isomeric Sugar with Special Reference to Galactose.**

*H. J. Hamburger, Biochem. Ztschr., 128:185, Berlin, March 7, 1922.*

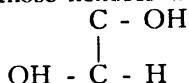
In the employment of physiologic nutrient solution of suitable composition (Hamburger-Brinkmann's modified Ringer's solution) glucose is retained by the renal glomerular membrane. In this, the solution's calcium-ion content plays the principal part. As other crystalloids, such as sodium chlorid, sulphates and phosphates pass through

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the glomerular membrane, this behavior was considered noteworthy. The phenomenon could not be due to the size of the molecule as raffinose and lactose, though possessing larger molecules, nevertheless pass through the membrane, so that it must be ascribed to a special configuration of the glucose molecule. As a matter of fact it was found that isomeric fructose and mannose passed to a considerable extent. The question arises, which atomic group in the glucose molecule should be held responsible for the retention. For that reason a number of isomeric and stereo-isomeric sugars were investigated as regards their behavior toward the kidneys. The solution contained sodium chlorid, 0.5%, potassium chlorid 0.01%, calcium chlorid 0.04% and sodium bicarbonate 0.285%. Sugar was estimated by Bang's method. The arbitrary hypothesis was propounded that the group



effects retention, and that those hexoses with the group



pass through. If this hypothesis were correct the pentoses could be arranged in two groups, one of which is retained and the other passes through. Thus, the hypothesis demanded retention of (1) d-glucose, (2) l-mannose, (3) d-galactose, (4) l-arabinose, (5) l-xylose and (6) d-ribose, but only partially, while l-mannose and l-arabinose passed through completely. No retention was to be expected in the case of (7) l-glucose, (8) d-mannose, (9) d-glucosamin, (10) d-arabinose, (11) d-xylose. Actually all these substances passed through, only d-xylose being particularly retained. It would have been desirable to test the hypothesis for other sugars but no further stereo-isomeric hexoses and pentoses or tetroses were available. For the present, however, the hypothesis must not be considered proved. Other hypotheses based on differences in surface tension or viscosity of the different sugars had to be abandoned by reason of negative experimental results. The conception of the adsorption of sugar in the kidney substance was subjected to thorough experiment without result. The peculiar behavior of galactose, which sugar occupies a middle position, i. e., it is partly retained and partly transmitted, was investigated. This sugar contributes materially to the formation of lactose and participates in the building up of cerebrosids. Two explanations seemed possible. First, that the concentration in which galactose was employed exceeded the tolerance of the kidneys for the same. But it transpired that, no matter what concentration was used, the substance was never retained completely, unlike d-glucose. A part was always retained, about one-half. The second explanation therefore appeared more important, namely that two substances are present in the galactose solution, one of which does and the other does not pass through the glomerular membrane. This view finds support in the fact that galactose solution occurs in an  $\alpha$  and in a  $\beta$  form, and in the further fact that the proportion of the retained to the passed portion of galactose is about the same as the proportionate amounts of the two modifications in the nutrient solution.

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**Variable Permeability with Special Reference to Stereo-Isomeric Sugars. An Attempted Interpretation of This Variability.**

*H. J. Hamburger, Biochem. Ztschr., 128:207, Berlin, March 7, 1922.*

Blood flowing through the capillaries takes up carbon dioxid which is removed in the lungs. In this process chlorin enters the blood-cells, the alkalinity of the blood fluid is increased and considerable swelling of blood-cells at the expense of the serum takes place, whereby the concentration of albumin and other serum bodies is also increased. Each respiratory act is accompanied by rhythmic changes as a result of the altered permeability of blood-corpuses. Reversible swelling and exchange of constituents under the influence of carbon dioxid are, however, not confined to blood-corpuses but occur likewise with other cells, such as spermatozoa, esophagus epithelium, liver cells and kidney epithelium. In the course of experiments it was found that glomerular epithelium is capable of retaining the blood sugar when an artificial modified nutrient solution of the following composition is employed in place of the customary Ringer's solution: sodium chlorid 0.5%, sodium bicarbonate 0.285%, potassium chlorid 0.01%, calcium chlorid 0.04%. In this the free calcium-ions are the important factor. Glomerular epithelium in contact with this modified Ringer's solution is impermeable to glucose. That is due to surface tension which is governed by the amount of free Ca ions. Whether or not a membrane is permeable for glucose depends, however, on the form of the aqueous pores. In the case of the kidney a perfusion solution with a Ca concentration of 9 mg. per liter is physiologic, i. e., it renders glomerular epithelium impermeable to a normal glucose concentration. If Ca concentration is less or greater the sugar passes through. Other organic substances may also influence permeability in a reversible manner. In the case of mutarotatory sugar, for instance galactose, which occurs in two modifications ( $\alpha$ ,  $\beta$ ), this slight difference in the structure of the two molecules may be the reason why the one modification does and the other does not pass through the membrane. At the earliest stage of blood coagulation the blood-corpuses become permeable to glucose. Substances foreign to the blood, like phlorizin, may change the permeability of the glomerular membrane reversibly. It is certain that products of internal secretion circulating in the blood influence the permeability of cells, but whether structural changes of the ultra-microscopic pores of the cellular surface are also involved in this, must be determined by research.

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**The Significance of Hydremia in the Secretion of Urine.**

*Harry Bakwin, Am. J. Physiol., 60:343, April 1, 1922.*

During the course of some studies on the fluid treatment of infants with diarrhea, data on the relation between blood concentration and urine output were obtained by Bakwin. In the method followed normal male infants were given 30 to 35 c.c. fluid per kg. body weight and the urine collected for four hours. Blood samples for refractometric determination were taken immediately before and at frequent

intervals after the fluid was drunk. The water was sweetened with a little saccharin. Saline was given by gavage. The serum concentration was determined with the Abbé refractometer. The method of Robertson was used to determine the refractive index of the nonprotein substances of serum. The amount of urine voided was carefully noted. It was observed that after water drinking, a moderate hydremia occurred without diuresis. After saline drinking, there was a marked blood dilution and oliguria. In infants hydremia alone does not necessarily cause diuresis.

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**Experimental Polyuria.**

*McMicken Hanchett, Am. J. M. Sc., 163: 685, May, 1922.*

Hanchett's experiments, carried out on dogs, consisted in: (1) stimulation of the anterior and posterior lobes of the hypophysis by varying degrees of heat, by trauma, by a cone-shaped plug of beeswax pushed into an opening in the bone, or by induced electric current; (2) herniation of the gland through dural opening; and (3) traction on the base of the brain with as little trauma as possible to the gland. The effect of pituitrin and epinephrin on experimentally produced polyuria was also studied. Hanchett concluded that experimental lesions of the hypophysis itself are not constant in the production of polyuria, but that some additional element is the determining factor. Experimental lesions of the hypophysis (similar to those producing only negligible excretory changes), when associated with traction upon its attachment to the floor of the third ventricle, however, uniformly caused polyuria, the degree of polyuria being roughly in proportion to the amount of traction. Polyuria associated with hypophyseal changes is due to stimulation of the regional base of the brain, floor of the ventricle and corpora albicantia. Clinical evidence, although indefinite, also indicates that neither increased nor decreased activity of any portion of the hypophysis is uniformly associated with polyuria. It was found that intravenous injections of pituitrin temporarily lowered the excretory rate in a polyuria experimentally produced in dogs, while intravenous injections of epinephrin had no effect on a polyuria of this type.

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**The Influence of Drugs on Kidney Function.**

*E. Starkenstein, Arch. f. exper. Path. u. Pharmakol., 92: 339, Leipsic, March 10, 1922.*

The increased excretion of urine due to adrenalin is further augmented to a considerable extent by atophan. Experiments on rabbits showed, however, that neither glycemia nor glycosuria was increased in rabbits previously treated with atophan as a result of the adrenalin effect. The amounts of sugar excreted also remained unaltered after injection of a 50% glucose solution following administration of atophan, although the volumes of urine had increased considerably. Moreover, in diabetic patients and in an auto-experiment, no increase in glycosuria could be determined after ingestion of 110 gm. glucose in spite of atophan. Water elimination is therefore independent of glycosuria.

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It seemed probable that the initially observed diuresis depended on the disposable water. From a study of water diuresis it appeared that the urine volume depends on: (1) the amount of intake either distributed over the whole day, or ingested at one time; (2) the quantitative composition; and (3) the manner of application of the amount of ingested liquid. As regards (1): Auto-experiments showed that with a total intake of 2 liters water per day the urine volume amounts to about 1400 c.c. In a deprivation period of twelve hours 500 c.c. urine are still excreted, while on the other hand the increase of urine volume is inconsiderable with a total intake of liquid amounting to 3300 c.c. distributed over the whole day. But if large amounts of water are given at one time (water experiment) the total volume of liquid ingested is excreted in the urine in four hours. Regarding (2): Of 1 liter drinking water, 900 c.c., and of 1 liter sodium chlorid solution (1%), only 300 c.c., are excreted in five hours (the same result is obtained with ingestion of Ringer's solution). A similar observation is made in the rabbit. Isotonic fluid therefore comes to rest in the body depots and is then slowly eliminated, whereas hypertonic and hypotonic solutions are eliminated by the kidney. For these reasons water taken with meals is not eliminated immediately because it becomes isotonic in contact with the nutrient salts. Regarding (3): Experiments on rabbits show that, following injection of atophan, if 100 c.c. Ringer's solution be introduced by mouth, 230% fluid is excreted within twenty-four hours; if 150 c.c. be injected intravenously, 150% fluid is excreted in a few hours; and if 100 c.c. be injected subcutaneously, 120% fluid, distributed over forty-eight hours, is excreted. In untreated animals the proportion of excretion of orally, subcutaneously and intravenously administrated Ringer's solution is as 1:1.5:2.2. On the strength of these results the action of atophan in man was studied. Of a single water ingestion of 1000 c.c. 74% was excreted by the normal individual, after atophan 82%. After drinking Ringer's solution the normal individual excreted 16% and after atophan 46%. Finally, it was possible to increase diuretin diuresis and to initiate the urine excretion by atophan with a single administration.

The excretion of various urinary substances after atophan was studied. It was found that menthol favors the excretion of uric acid and acetone independently of diuresis, whereas excretion of chlorids and of sugar is influenced by atophan concurrently with diuresis. On the basis of this fact the manner of action of atophan is discussed and the probability conceived that it removes arrest of kidney secretion by paralysis of the sympathetic and promotes, in this way, the already initiated diuresis. Therapeutically it is of importance, in any event, that atophan is capable of supporting the action of diuretics.

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**The Function of the Renal Calices.**

*H. Haebler, Ztschr. f. Urol., 16: 145, Leipsic, April, 1922.*

Haebler supplements an observation of Wassink, who saw contraction waves pass over the dilated pelvis (beginning at the calices) of a hydronephrotic kidney that had just been extirpated. According to Henle, there is a deposit of sphincter muscle at the base of the papilla

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in man, the contraction of' which contributes toward the emptying of the urinary tubules into the papilla. In addition, there is, according to Disse, a marked traction of the sphincter fibers at the narrowest portion of the renal pelvis, that is at the insertion of the calyx into the renal pelvis, which constrict the opening and probably can close it entirely.

Histologic examinations were made in the rabbit, cat, dog, goat, sheep, calf, cattle, pig and finally man: the latter showed powerful sphincter fibers at the base of the papillae, and nearer the apex of the papilla less powerfully developed circular muscle strands, which no doubt have the function of establishing more or less resistance against noxa penetrating toward the papillary ducts. (Superior sphincter of the papilla representing the "expulsive muscle", and inferior sphincter of the papilla, the "protective muscle.") An attempt was made to observe the peristaltic waves in the living animal, by making a nephrotomy with careful digital compression of the pedicle vessels *in situ* in guinea-pigs, rabbits and dogs; circular contractions of the mucosa of the renal pelvis were observed in both kidneys of 2 cats, the waves becoming lost in the renal pelvis. These peristaltic motions continued for a few minutes after the removal of the organ and could also be produced by slight mechanical and chemical stimuli.

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#### Physiologic and Pharmacologic Studies of the Prostate Gland.

#### IV. Response of Prostatic Muscle to Drugs.

*David I. Macht, J. Urol., 7: 407, May, 1922.*

The motor and secretory innervation of the prostate gland is supposed to be derived from the hypogastrics and the nervi erigentes, but stimulation of these failed to produce secretion after ejaculation of prostatic secretion had followed stimulation of the nervus erigens, showing that the latter supplies the musculature but not the glandular portion of the prostate. It was also found that the prostate musculature is devoid of parasympathetic terminals: it responded to treatment with epinephrin and ergotoxin on the one hand, and on the other (except in the rabbit) not to parasympathetic drugs.

The effects of various drugs were studied on strips of surviving excised prostate glands of different animals. There was a prompt contractile response to barium chlorid and relaxation to papaverin hydrochlorid, indicating the presence of muscle tissue. There was a distinct response to the treatment with epinephrin and ergotoxin, but none (with the exception of the rabbit) to pilocarpin, physostigmin, muscarin and atropin, arguing for a true sympathetic innervation of the prostate gland.

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#### Anoxemia and the Increased Electric Excitability of the Neuromyone.

*N. Morris, Brit. J. Exper. Path., 3: 101, London, April, 1922.*

The object of this work was to determine the cause of the increased electric excitability often manifested by the neuromyone. The method

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used for measuring the strength of current causing contraction was that employed by Noël Paton, Findlay and Watson, who give a criticism of its limits of accuracy. The methods of estimating various changes in the blood were those of the alkaline reserve (by the Van Slyke method), the hydrogen-ion concentration (Bayliss), and the oxygen content of the blood (Barcroft's differential method). Cats and dogs were used in all the experiments. Electric reactions taken several times before the injection was commenced showed that neither the anesthetic nor the operation had any effect on the reactions. Venous and arterial blood was withdrawn for examination without causing any alteration in the electric reactions.

A mass of experimental data with accompanying tables and the results of earlier workers are recorded in connection with the effects of various compounds, acids, alkalies, etc. on the electric excitability of the neuromyone. The results of these experiments were as follows: The excess of sodium is nothing more than a predisposing factor in the production of an increase in the electric excitability. While injection of calcium salts has a sedative effect on the neuromyic excitability, the present work lends no support to the view that diminution of calcium is the underlying cause of increased excitability. The amount of calcium in the blood shows no change when the excitability is increased by certain methods. The administration of HCl, lactic acid, and phosphoric acid leads to marked diminution of electric excitability, and renders the blood mesonectic.  $\text{Na}_2\text{CO}_3$ , NaOH and  $\text{NH}_4\text{OH}$  increase electric excitability, produce an alkalosis and diminish the supply of oxygen to the tissues. Asphyxia, lowering of the temperature and anemia, each causes an increase in excitability and a diminished supply of oxygen to the tissues. Administration of cyanide induces an increased electric excitability of the neuromyone as well as other symptoms of profound oxygen want. Small doses of alcohol have practically no effect either on the electric excitability or on the oxygen supply, while large doses cause a rise in the former and a fall in the latter. The alkaline reserve is diminished. Histamin produces an increased electric excitability as well as an anoxemic condition. A general survey of these results justifies the following conclusions: (1) An increase in the electric excitability occurs independently of change in the alkaline reserve. (2) Any experimental method whereby an anoxemia is produced (a diminution of alkalis, cyanides, histamin or asphyxia) causes increase in the electric excitability. (3) Any increase in the electric excitability is accompanied by diminished supply of oxygen to the tissues. (4) Anoxemia is the essential condition underlying increased electric excitability of the neuromyone.

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**Physiologic and Colloidochemical Researches on the Mechanism of the Contraction of Striated Muscle Induced by Poisons..**

*Otto Riesser and S. M. Neuschlossz, Arch. f. exper. Path. u. Pharmakol., 92: 254, Leipsic, March 10, 1922.*

Experimental procedure: Frogs' gastrocnemius muscles were subjected to the action of different concentrations of the selected substances, the fillings being recorded graphically. Nicotin was examined (Sec. 1—Page 1051)

first in the strength 0.5: 1000 after it had been neutralized with hydrochloric acid. Results: In analogy to the action of acetylcholin, a brief primary excitation contracture was observed, which was soon replaced by relaxation. Paralysis from electric stimuli begins simultaneously. Contractile capacity is restored only after prolonged washing in Ringer's solution. Explanation: Nicotin first stimulates the neural region substance; if the injury to the contractile substance continues to predominate, paralysis and relaxation of the muscles must set in, in spite of prevailing stimuli. Curare, as well as atropin and novocain, removes the excitation contraction due to nicotin (analogous to acetylcholin) but after previous treatment with these substances nicotin rigidity (injurious contraction) of the muscle sets in slowly. Probably atropin displaces the nicotin, whereas novocain exerts an action on the muscle colloids. A similar antagonistic action to that of atropin or novocain toward nicotin is displayed by veratrin. If the muscles are previously treated with atropin or novocain no veratrin contraction takes place. This fact alone points to a physicochemical mechanism of this process. Finally, the authors were able to cause excitation contraction before paralysis with potassium salts ( $K_2SO_4$ ), which however cannot be influenced antagonistically either by atropin or novocain. All the substances mentioned here act on the receptive substance, which is probably identical with the preterminal network described by Boeke.

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**Functional Evidence of the Phylogeny of the Nervous System as Shown by the Behavior and Resistance of the Developing Rat to Strychnin.**

Erich W. Schwartz, *J. Pharmacol. & Exper. Ther.*, 19: 273, May, 1922.

Strychnin sulphate, U. S. P., found by chemical tests to be free from brucin, was used in all experiments. The lower concentrations employed were made from a freshly prepared solution of 0.1% strychnin sulphate in 0.9% NaCl. The injections were made by means of tuberculin syringes into the subcutaneous tissue of the ventral abdomen wall. In case of very small rats, the needle was inserted in the thigh, as this circuitous route helped to prevent leakage. The dosage was always administered on the basis of body weight. All rats were placed in small wire-bottomed cages, which offered them an opportunity for grasping. The importance of this seemed to be considerable, since it was preferred by the rats and since instances of premature and nonfatal spasms were apparently fewer. A more constant lethal dose was thereby obtained. When necessary, the smaller rats were protected from cold by suitable application of heat. Some time after birth the rat began to lose its natal resistance to strychnin. During this interval, however, it still possessed the lower vertebrate type of reaction, namely, the tendency to have numerous spasms which were separated by periods of relaxation and apnea, even though more than the lethal dose had been administered. Several days after the opening of the eyes, after the rat had emerged from the crawling stage, it usually acquired the adult type of reaction, namely the tendency to but one fatal spasm. At this time the lethal dose was at its lowest limit, or 0.5 mg. per kilo.

Subsequently the rat acquired a postnatal immunity, which increased up to the time of maturity, at which time it had an absolute value of 6 times that exhibited on emergence from the crawling stage.

The facts are indicative that the developing central nervous system of a rat (and presumably of other mammals) passes through certain functional stages of development from the lower prototype to the higher forms, which are just as definite and as important functional evidence of the phylogenetic development of the nervous system as morphologic, physiologic or psychologic evidence.

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**Studies on the Visceral Sensory Nervous System. XI. The Action of Cocain and Aconitin on the Pulmonary Vagus in the Frog and in the Turtle.**

*Nathaniel Kleitman, Am. J. Physiol., 60: 203, April 1, 1922.*

This report comprises the results of experiments designed to elucidate the rôle of the afferent fibers of the vagus in the reflex and tonic activity of the amphibian and reptilian lung. Cocain and aconitin were the drugs used. In the experiments with frogs, the contractions of the lung were recorded by inserting a cannula into the tip of the lung and connecting it with a water manometer or a sensitive tambour. The animals were always decerebrated and prepared according to the method of Carlson and Luckhardt. Each lung was insulated by means of sheet rubber so that no drug could get to the neighboring viscera. Drugs were injected intravenously through a cannula inserted into the median abdominal vein. To prevent a drug injected intravenously from reaching the lung used as a control, the pulmonary artery on that side was ligated. In such cases methylene-blue was injected at the end of the experiment and the absence of blue in the corresponding lung was used as a test of the efficacy of the method. As a general procedure only one vagus was used, the other being ligated and the lung on that side allowed to go into hypertonus.

In the experiments with turtles the left lung was isolated for recording lung contractions, the other being left in communication with the outside, through a tracheal cannula, for the purposes of respiration. Preparation of the decerebrated animal for lung contractions, as well as the method for recording the lung contractions, was the same as for the frog. For the local application of cocain both vagi were isolated in the neck for about 2 in. A piece of cotton the size of a small pea was saturated with the solution, the middle portion of the isolated nerve was insulated with a strip of sheet rubber, the cotton placed on the nerve, and the rubber tied with a thread tight enough to express the solution on the nerve but not so tight as to compress the nerve itself. The stimulating electrodes were then applied to the proximal or distal portion of the nerve about 1 cm. away from the place where the drug was applied. For intravenous injections the external jugular vein was cannulated. In the turtle the presence of the normal spontaneous lung contractions depended on outside conditions. During the second half of June and the very last week of August all turtles used showed spontaneous contractions of the lungs as soon as the preparations were ready for recording. During July and the greater part of August not a single turtle could be found to exhibit this phenomenon.

The experiments with cocaine on frogs included: (1) intravenous injections of cocaine; (2) intra-arterial injections of cocaine; and (3) local application of cocaine to the lung. The experiments on turtles included: (1) intravenous injections of cocaine and (2) the application of cocaine to the trunk of the vagus. The experiments with aconitine on frogs included: (1) intravenous injections; (2) intra-arterial injections; and (3) local application of the drug. The experiments with aconitine on turtles were limited to intravenous injections.

Results show that the intravenous injection of 1 mg. cocaine hydrochloride will abolish the lung and heart reflexes in the frog by paralyzing or greatly depressing the efferent endings of the vagus. The lung escapes from the inhibitory control of the vagus for the same reason. Whether the efferent endings are similarly affected has not been established. A much larger dose of cocaine is necessary to produce an escape of the lungs by paralyzing the vagus center. Intravenous injection of cocaine will produce slowing of the heart, if the dose is small (1-2 mg.). Larger doses cause complete or partial heart block. Local application of cocaine to the lung of the frog had the same effect as intravenous injection of the drug. Intravenous injection of cocaine abolishes the spontaneous lung contractions in the turtle by paralyzing or depressing the efferent motor nerve endings of the pulmonary vagus, essentially the same effect as that observed in the frog. As the spontaneous lung contractions in the turtle disappear after a 2-5% cocaine solution is applied directly to the vagus trunk in the neck, it may be inferred that the efferent impulses from the lung-motor center are blocked by the cocaine. Stimulation of the vagus above the point of application of the drug produces a feebler contraction of the lung than stimulation below that point. This is not due to blocking the conduction in some fibers, but rather to a depression of the conductivity in all the fibers. The afferent fibers of the pulmonary vagus were found to be more resistant to the action of cocaine than efferent fibers.

Concerning the action of aconitine it was observed that minute doses of this drug paralyzed the efferent inhibitory endings of the pulmonary vagus in frogs, and larger doses paralyzed the vagus center, thus resembling the action of cocaine on the same structures. Intravenous injection of aconitine paralyzes the respiratory center in turtles and thus indirectly abolishes the spontaneous contractions of the lungs. Aconitine also produces a state of contracture in the turtle's lung.

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**Studies on the Visceral Sensory Nervous System. XII. The Response of the Isolated Esophagus of the Frog and the Turtle to Certain Drugs.**

*Z. Bercovitz, Am. J. Physiol., 60: 219, April 1, 1922.*

This work was undertaken to determine whether further light on the motor control of the esophagus might be secured by the study of the reaction of isolated preparations of the esophagus to the so-called neurotropic and myotropic drugs. In the experiments on the frog the entire esophagus was used. In studying the circular system the esophagus was suspended as a ring in a muscle warmer and connected with German silver wire hooks to a delicate heart lever which recorded on

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a slowly moving drum. It was found necessary to turn the esophagus inside out before any dependable reactions to the drugs could be obtained. In the study of the longitudinal neuromuscular mechanism one end of the esophagus was attached by means of a small clamp to a fixed point in the muscle warmer and the other with a similar clamp by a silk thread to a delicate heart lever. The weight of the clamps was carefully counterbalanced. The fluid in the muscle warmer was changed by displacing it from below, thus preventing exposure of the tissue to the air. In the experiments with the turtle, after removing the plastron the entire esophagus and stomach were carefully cut away from their surrounding tissues. In studying the circular system 2 methods of suspending the preparations were used: (1) the same as in studying the circular fibers of the frog esophagus; (2) that of applying small clamps to the esophagus so that the direction of work of the muscle was the same as when it was used as a ring. When studying the longitudinal system the clamps were used entirely with strips of about 1 cm. long.

Results show the action on the preparations described above, of nonaerated Ringer's solution, aerated Ringer's solution, oxygenated Ringer's solution, adrenalin, pilocarpin, nicotin, atropin, histamin, and pituitrin. With the frog's esophagus it was found that tonus and spontaneous contractions are maintained only in well oxygenated Ringer's solution. Atmospheric air cannot be substituted for pure oxygen. Adrenalin caused a uniform inhibition of the longitudinal system and stimulation (66% of experiments) or inhibition (33% of experiments) of the circular system. The adrenalin action seemed to be more marked after atropin. Pilocarpin stimulated both circular and longitudinal systems. Atropin counteracts this effect of pilocarpin. Nicotin was found to cause a primary inhibition followed by stimulation of the circular and longitudinal systems. Histamin and pituitary liquid (Armour's) caused uniform inhibition of the circular and the longitudinal systems. In the experiments with the turtle's esophagus it was found that the longitudinal and circular systems at all levels reacted uniformly. Administration of adrenalin caused a profound and lasting stimulation usually preceded by a temporary inhibition. Atropin had no effect on this adrenalin action. Pilocarpin caused a temporary inhibition followed by a marked stimulation. Nicotin caused a profound inhibition and histamin was followed by an increase in tone.

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**A Study of the Regeneration of the Autonomic Fibers in the Vagus Nerve of the Sheep.**

*Stanley Ross Burlage, Am. J. Physiol., 60:350, April 1, 1922.*

To date all of the work upon regeneration of the autonomic fibers in the vagus has shown that the cardiac fibers in the right vagus of the dog may in some instances again become functional in from 300 days to 20 months, and that similar results may follow severing the left vagus of the rabbit in from 3 years and 8 days, to 3 years and 38 days.

In December, 1920, 5 sheep, 4 ewes and 1 ram, were put under observation. The normal heart and respiration rates of each animal being determined, a unilateral vagotomy was performed upon each sheep.  
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In 2 ewes the left vagosympathetic trunk was cut and in the remaining 2 ewes and the ram the right vagosympathetic was severed. Only one of the ewes lived until Dec. 8, 1921. In this animal it was then found that ligature and cutting of the previously severed vagosympathetic nerve trunk, followed by stimulation of the peripheral end with weak and strong induced current, produced no effect upon the heart rate. It was therefore inferred that there is no regeneration of the efferent autonomic fibers of the vagus in the sheep or that regeneration is not complete in 12 months.

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The Trophic Influence of the Sympathetic System on the Diaphragm.

*Ken Kuré and Masuo Shimbo, Ztschr. f. d. ges. exper. Med., 26:190, Berlin, March 6, 1922.*

A certain relationship between the sympathetic and muscular nutrition must be assumed to exist in general, namely, in the sense that the sympathetic indirectly influences muscular nutrition by its influence on vascular nerves. But up to the present, no one has been able to show that the sympathetic exercises a direct trophic influence on transversely striated muscle. In order to study this the authors investigated the structure of the phrenic nerve. It consists of sympathetic and cerebrospinal fibers. The latter arise in man in the third to fifth cervical roots; the former in the uppermost thoracic and lowest cervical ganglia. Near the hilum of the lung both kinds of fibers are seen in preparations stained by Weigert's and Van Gieson's methods. The experiments were conducted on dogs and apes, and the few that survived any length of time were examined histologically. If the cerebrospinal roots of the phrenic nerve be divided the diaphragm becomes atrophied from inactivity. Two or three months after operation the histologic signs are slight atrophy and increase in nuclei. Evulsion of the phrenic nerve produces diaphragmatic atrophy and degeneration. Four months later the musculature is already greatly degenerated and has the appearance of connective tissue. Histologically there is observed atrophy, increase of nuclei, hyaline and fatty degeneration. Isolated atrophic muscular fibers may be seen for a considerable time. Finally, the pars lumbalis becomes affected in which the processes are never as intense. If the abdominal sympathetic be destroyed in addition to the phrenic nerve the same or even more intense atrophy results which may include the pars lumbalis. Destruction of the abdominal sympathetic and of the cerebrospinal roots of the phrenic nerve also causes atrophy in which the pars lumbalis participates strongly. Following eradication of the abdominal sympathetic alone, distinct changes are observed only in the pars lumbalis of the respective side, these being particularly distinct in young animals. The microscopical picture resembles that of progressive muscular dystrophy, though proliferation of fatty tissue is absent. The animals do not long survive extirpation of the cervical sympathetic. Accordingly, neither exclusion of the sympathetic fibers, nor of the cerebrospinal fibers, produces intense atrophy of diaphragm by itself. The influence of the sympathetic is not based on vascular paralysis. Inasmuch as Kuré, Shinosaki, Kishimoto, Sato, Hoshino and Tsukiji have shown recently that the facts observed in the case of the

diaphragm also apply to tonic innervation of the general voluntary muscles it is very probable that this relation of trophic innervation will possess general validity also for voluntary muscles.

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**Chemical Researches on Diaphragmatic Tonus.**

*Ken. Kuré, Minoru Maeda and Kozo Toyama, Ztschr. f. d. ges. exper. Med., 26:176, Berlin, March 6, 1922.*

The authors employed 34 large dogs in their experiments. Whereas, normally, the creatin content of the 2 sides of the diaphragm was the same, the diaphragm of the side on which the phrenic nerve and the sympathetic fibers were excluded showed less creatin content. Creatin was estimated as creatinin by Pekelharing's method. The purified muscle is boiled in 1% hydrochloric acid five hours, dealbuminized under neutralization with sodium bicarbonate, diluted and filtered. After concentration on the water bath, and addition of twice the volume of NHCl, it is heated in the autoclave half an hour at 115°. Creatinin is estimated by Folin's method. When only the sympathetic fibers were eliminated (the cervical sympathetic is isolated and extirpated up to the stellate ganglion, and the fibers trending from the celiac ganglion to the diaphragm are eradicated) the amount of creatinin in the diaphragm is likewise reduced. Division of the motor roots of the phrenic nerve (5-7 cervical nerve) increases the creatin content during the first three days and diminishes it on the fifth day. Evulsion of the right phrenic nerve and division of the motor root of the left phrenic nerve causes reduction of creatin in the right diaphragm after thirty days. The right cerebral cortex was excluded in 2 dogs and increase of creatin content on the left was noted after six to sixteen hours. From this it is evident that muscular albumin metabolism is regulated by the sympathetic. The objections raised to Pekelharing's views (muscular atrophy, circulatory disturbances) do not apply here because the former was examined a few hours after operation and the diaphragm is supplied by the intercostal vessels. The conditions produced by absence of motor fibers are not quite clear. Possibly the subsequent creatin decrease is already related to atrophy.

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**The Movement of Respiratory Air in the Pulmonary Alveolar Passages.**

*H. Dreser, Ztschr. f. d. ges. Med., 26:223, Berlin, March 6, 1922.*

With the aid of models and colored liquids or ammonia vapors, the author investigated how air is mixed on entering the lungs and what currents arise. It was shown that the most intimate mixtures are guaranteed when a stenosis occurs in front of the alveolar vesicle as represented actually by the alveolar duct, whose caliber is one-quarter that of the alveolus. If the expired air be divided into 2 portions, one of which corresponds to the air of the noxious space and the other and smaller portion to the alveolar air, the noxious space is determinable by means of corresponding measurements and gas analysis. The author describes calculations for this purpose, attempts geometrical representation (Sec. 1—Page 1057).

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tions and criticizes Bohr's theory of carbon dioxid "secretion" in the lung. It was found that the alveolar air is renewed in about 6 inspirations. The inspired air advances progressively and if it enters the alveolus it moves along the wall and again enters the bronchus only with the sixth inspiration. Noxious space is greatly increased in the presence of cavities. The determination of the most favorable form and size of the alveolar unit is attempted by mathematical calculations. Spherical alveolar spaces are said to possess the greatest capacity with an equal surface but are not dilatable and much space is lost. By means of differential calculus it is shown that a cylinder whose width is twice as great as its height would be required. But it has to be further considered that the air must remain in contact with the alveolar wall for a considerable time, so that an onward movement must take place, which may affect the form representing the optimum. The action of inhalants such as camphor, or the drinking of onion decoctions, as practised in household medicine, may possibly be explained by the fact that these remedies reduce the surface tension of the secretions which offer considerable resistance to the circulation of inspired air, in pathologic processes, in the narrow alveolar duct. The usefulness of oxygen inhalations is, however, taken at a low value.

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**Recording Respiration Frequency in Small Experimental Animals.**

*Werner Teschendorf, Arch. f. exper. Path. u. Pharmakol., 92:335, Leipzig, March 10, 1922.*

An apparatus for recording plethysmographically the inspirations of small animals, especially of mice and rats, is described. It consists essentially of a glass cylinder whose upper end is closed hermetically by a rubber cap; its lower end receives a tube connected with a Marey capsule. The animal's hind legs are tied together (the cord is fixed outside) while the fore legs are tied to the board to which the glass cylinder is attached. The rubber flap is provided with a narrow opening that firmly encircles the animal's body.

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**Studies on the Conditions of Activity of the Endocrine Glands.  
X. The Cardio-Accelerator Substance Produced by Hepatic Stimulation.**

*W. B. Cannon and F. R. Griffith, Am. J. Physiol., 60:544, May 1, 1922.*

A preceding paper presented evidence that stimulation of the hepatic nerves caused a substance to appear in the blood passing through the liver that accelerates the denervated heart and induces a rise of blood pressure. To investigate the nature of this pressor and cardio-accelerator substance, experiments were made on etherized cats. The inferior vena cava was then stimulated but an acceleration of the denervated heart did not result. Hence the accelerator agent, appearing when the hepatic nerves are stimulated, must be conveyed in the blood stream. This accelerator effect can be produced by reinjecting into the inferior

vena cava blood drawn from the hepatic veins during stimulation. In the author's previous work a cardio-accelerator effect was observed in many of the animals which were actively digesting, but it was slight if the animals were fasting or in poor physical condition. This difference suggested testing the effects of different classes of food. It was found that carbohydrate or fat was without influence on the effectiveness of hepatic stimulation in evoking a faster beat of the denervated heart. As a rule stimulation was most effective when the animal was digesting meat. The authors conclude that the substance which increases the rate of the denervated heart and raises the blood pressure is discharged into the blood stream when the hepatic nerves are stimulated and is possibly related to the protein masses stored in liver cells and discharged by adrenalin.

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**Physiology of Glands. Researches on Centrally Conditioned Alteration of Blood-Sugar Content and on the Influence of the Internal Ovarian Secretion on This Reaction. New Proof of the Internal Secretion of the Ovary.**

S. Takakusu, *Biochem. Ztschr.*, 128:1, Berlin, March 7, 1922.

Nervous and metabolic phenomena accompany decreased activity of the ovary. It is a question whether removal of the ovary induces a change in the reacting capacity of that part of the central nervous system which governs vegetative functions. Of all the vegetative functions which are influenced by the central nervous system the carbohydrate metabolism has been investigated most thoroughly. The method consists in influencing carbohydrate metabolism by central stimulation and comparing, under otherwise similar conditions, the reactions in animals before and after castration. This may be studied with diuretin, which alters the sugar content of the blood by stimulation of vegetative centers of the central nervous system. As the reaction to heat puncture is the same in ovariectomized as in normal animals, this method could not be employed to elucidate the eventual relations between the ovarian hormone and the central nervous system.

Sugar was estimated by Bang's micromethod. Diuretin was dissolved in 15 c.c. physiologic sodium chlorid solution, and 1.5 gm. was injected under the skin of the back. It was found that, following castration, the hyperglycemia produced by diuretin decreased more and more in course of time. As this hyperglycemia is conditioned centrally it may be assumed that the absence of the ovarian hormone lowers the sensitiveness of certain parts of the central nervous system. For the exact analysis of the experimental results parabiosis was also employed. It was shown that a castrated female when united to a normal female reacts more actively following diuretin injection. This constitutes proof of the internal secretion of the ovary, as parabiosis causes no alteration in the castrated animal other than an exchange of blood and lymph (slight in amount) between it and the animal that is in possession of its ovaries. When parabiotic union is dissolved, reduction of the reacting capacity to diuretin is observed in the castrated animals only after nine weeks, while after castration this becomes manifest in four or five weeks. Following removal of the ovaries intense atrophy of the uterus and of the vagina occurred. The reduction of hyperglycemia

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following diuretin injection is a sexually specific phenomenon in the female animal, and was not observed in the male. In the latter, manifestly, no alteration of the parts on which the diuretin reaction is dependent takes place.

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**The Relation of Splenectomy to Growth and Appetite in the Rat.**

*Arthur H. Smith and Leah Ascham, Am. J. Physiol., 60:250, April 1, 1922.*

The authors wished to obtain accurate data on the question of appetite growth after splenectomy. White rats were used and under ether anesthesia the splenic vessels were ligated en bloc when animals were about 40 days old. In the control rats an abdominal incision was made and the spleen drawn out and replaced, the whole operation simulating as far as possible the splenectomy. The rats were fed ad libitum upon the diet of purified materials described by Osborne and Mendel. Vitamin B was provided by the administration of 0.4 gm. dried brewery yeast daily. The tabulated results show that the splenectomized white rats gave no evidence of an increase in appetite or variation from the normal rate of growth.

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**Physiology of Glands. The Function of the Spleen. Especially in Normal and Increased Oxygen Requirement.**

*Leon Asher and Ernst Bernet, Biochem. Ztschr., 128:251, Berlin, March 7, 1922.*

The spleen plays a part in iron metabolism as well as in respiratory metabolism. It was attempted to gain an insight into splenic physiology from the urinary secretion in normal and splenectomized animals in combination with experimentally produced oxygen deficiency. It was desired to ascertain whether with reduction of the respiratory pulmonary surface compensatory acid regulation is observable by increased ammonia excretion in the urine and whether total urinary nitrogen is altered. Four experimental series embraced estimation of daily ammonia, ammonia nitrogen and total nitrogen (1) in normal animals' urine, (2) in normal animals with experimentally increased oxygen requirement or with oxygen deficiency, (3) in splenectomized animals, and (4) in splenectomized animals with experimentally increased requirement or oxygen deficiency. Rabbits were accustomed to milk diet, on which a constant urine volume was also obtained. Ammonia was estimated directly and total nitrogen by Kjeldahl's micromethod. Oxygen deficiency was produced experimentally by means of artificial unilateral pneumothorax. (1) In normal rabbits no increase of ammonia occurs in urine with increased oxygen requirement. (2) Splenectomy may be followed by alteration of ammonia content in urine. (3) The spleen is able to influence ammonia excretion in urine but need not do so. (4) Increased oxygen requirement is not followed by alteration of ammonia content in urine in splenectomized rabbits. (5) Splenectomized rabbits excrete more nitrogen in the urine than normal ones. Protein metabolism is thus greater in splenectomized than in normal

rabbits. In the presence of the spleen protein metabolism is accordingly less and splenectomy is followed by an increase. Therefore the spleen exercises a regulatory influence on metabolism in the sense of economy. (6) With increased oxygen requirement, nitrogen excretion is increased in splenectomized rabbits. Under these impeded conditions increased protein metabolism is rendered more evident than with splenectomy alone. The results of Danoff's researches on respiratory metabolism in rats and Richet's on splenectomized dogs were confirmed by these researches.

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**The Relation of the Adrenals to Fatigue.**

*F. A. Hartman, R. H. Waite and E. F. Powell, Am. J. Physiol., 60:255, April 1, 1922.*

The authors tested the ability to work and to withstand fatigue, and in one instance the effect of pregnancy, in animals (cats) with a reduced epinephrin output. Many of the animals used were observed for some time and were tested before the operation. In most instances the removal of one adrenal and denervation of the other took place at one operation, the abdominal path being used. To prevent infection, regular hospital routine was followed. The ability of the animals to work and to withstand fatigue was tested by the treadmill. In their later work the authors used the denervated eye as a possible test for epinephrin in the work tests. Normal cats usually gave a dilatation of the denervated pupil accompanying work in a treadmill. This denervation is brought about by removal of one of the superior cervical ganglia. Spurts of work are accompanied by greater increases in the dilatation; the same cat will work harder and travel farther when such dilatation is present. The dilatation of the denervated pupil accompanying fatigue is absent in animals deprived of both adrenals or possessing but a single adrenal and that completely denervated. Such dilatation is probably caused by epinephrin. Cats possessing but a single adrenal, and that denervated, were found to undergo a period of ill health more marked than that of control animals. During this period the working power is very much decreased, but after regeneration of some of the nerve fibers, health and power to work are regained. These results indicate in all probability that epinephrin plays a very important rôle in increasing muscular work and delaying the onset of fatigue.

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**Studies on the Conditions of Activity in Endocrine Glands.  
IX. Further Evidence of Nervous Control of Thyroid Secretion.**

*W. B. Cannon and P. E. Smith, Am. J. Physiol., 60:476, May 1, 1922.*

The authors have shown that the denervated heart is remarkably stable in its performance and is unaffected by any but thermal changes and chemical agents brought to it in the blood stream. Since it manifests characteristic increments of rate when the adrenal medulla or the liver is stimulated, it was believed that another typical change might be demonstrated if thyroid were added to the adrenal effect. Accordingly (Sec. 1—Page 1061)

the heart was isolated from the central nervous system without disturbing the nervous connections of the thyroid gland. It was then found that gentle massage of the thyroid gland in these animals (cats) for three minutes caused an increased rate of the denervated heart. Massage of the submaxillary gland did not cause this effect. This augmentation of the heart rate occurred in the absence of the adrenal glands. It was also demonstrated that stimulation of the cervical sympathetic trunk as it leaves the stellate ganglion induces a similar augmentation of the rate of the denervated heart which does not occur if the thyroid gland has previously been removed.

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**The Secretory Action of the Pancreas in Relation to the Thyroid Gland. I. The Effect of Thyroid Feeding in Rats upon the Secretory Action of the Pancreas.**

*Hirotoshi Hashimoto, Am. J. Physiol., 60:357, April 1, 1922.*

In the author's investigation, white rats of similar size were divided into groups to be fed with different quantities of thyroid, and the changes of the secretory action of the pancreas in the animals of different groups were compared. After the desiccated thyroid powder (made from fresh ox thyroid glands) had been fed for a certain length of time, the animals were killed by chloroform and bled. The pancreas was removed in one piece, weighed and an extract of it made for the determination of the amylase content. The entire small intestine was removed, a solution of intestinal juice made and its amylase content determined. The tabulated results show that feeding animals comparatively large quantities (0.2 to 0.5 gm.) of thyroid daily, notably interferes with the secretory action of the pancreas. On the contrary, feeding comparatively small quantities causes a fair increase in pancreatic function.

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**The Secretory Action of the Pancreas in Relation to the Thyroid Gland. II. The Effect of Thyroidectomy in Rats upon the Secretory Action of the Pancreas.**

*Hirotoshi Hashimoto, Am. J. Physiol., 60:365, April 1, 1922.*

The author wished to determine if such amounts of thyroid autacoid as are passed by the normal gland into the general circulation (blood) exert an excitatory effect upon the secretory action of the pancreas. Accordingly experiments were made upon albino rats to ascertain the effect of thyroidectomy upon the secretory action of the pancreas. The dietetic and environmental conditions of the animals during the experiments and the methods of determining the secretory action of the pancreas were identical with those already described by the author. It was found that the removal of the thyroid glands in albino rats causes a decrease in the secretory action of the pancreas, the change being evident within two weeks after the operation, when no compensatory mechanism for the lost glands has yet been evolved.

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**The Rôle of the Thyroid Gland in Heat Regulation and Fever Metabolism.**

*E. Grafe and E. von Redwitz, Hoppe-Seyler's Ztsch. f. physiol. Chem., 119:125, Berlin, March 14, 1922.*

The parallelism of the height of the total metabolism and body temperature with the anatomic structure and function of the thyroid is made evident by Adler's experiments on hibernating animals. In order to gain an insight into the rôle of the thyroid in heat regulation in warm-blooded animals, it was possible to employ comparative regulation experiments in normal and thyroidectomized animals, or the testing of the regulatory capacity after combined thyroidectomy and division of the dorsal portion of the spinal cord. For research fasting dogs were employed which were subjected, before and after thyroidectomy, to temperatures of 20°, 14°, and 27-30° during respiratory experiments lasting eighteen to twenty-four hours. The customary daily calculations of the respiratory experiments were made. The experiments showed that the absence of the thyroid has no appreciable adverse influence on chemical heat regulation. The thyroid, therefore, obviously does not possess the great importance in regulation that might be expected from other researches. The results of these experiments make it improbable that combined division of the dorsal spinal cord and thyroidectomy removes chemical heat regulation. In one experiment it was shown that fever metabolism in the thyroidectomized dog proceeds in precisely the same manner as in the intact animal.

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**The Effect of Thyroid Feeding on the Bone-Marrow of Rabbits.**

*R. K. S. Lim, B. B. Sarkar and Jane P. H. Graham Brown, J. Path. and Bacteriol., 25:228, Edinburgh, April, 1922.*

In an endeavor to determine the part played by the bone-marrow in the causation of the variable changes of the circulating blood-corpuscles after thyroid feeding, rabbits of 3 series of weights were used: 500-750 gm., 1000-1500 gm., and 2000-2500 gm. Desiccated thyroid powder (mixed with meal mashed) was given in doses varying from 0.25 gm.-1 gm. per day. Some of the animals died from the dose and others were killed mechanically. Sections of their bones were fixed, parafined, sectionized and stained. Romanowsky combinations proved to be the most useful stains. The Thoma-Zeiss hemocytometer was used for enumeration of blood-corpuscles. Differential counts of the white corpuscles were made with Leishman-stained films. In the enumeration of the marrow-cells differential counts from the stained section were made. A number of squares were carefully drawn with Indian ink on a coverslip which was afterwards inserted in the middle of the eye piece, by adjusting the tube length, using an oil immersion-lens and a stage micrometer. The microscope was set so that each square represented an area of 0.0025 sq. mm. which was found the most convenient for counting. The technic was duplicated each time. Sections cut at 5 microns were counted.

The detailed results of each series of experiments are clarified by plotted curves of the marrow counts of the rabbits of the various weights, tables of the marrow counts and plates showing sections of the bones. In the young rabbits the bone-marrow contained fewer cells and more polymorphs in proportion to small mononuclears, than the adult animals. In young rabbits an increase of the polymorph percentage and a decrease of the small monocellular is very noticeable after thyroid feeding. This is the reverse in older animals even to a subnormal percentage of polymorphs and the mononuclear percentage may be above normal. The actual number of polymorphs rises and falls with the percentage figure, but no decrease below the normal is ever found even after prolonged feeding. The total number of marrow-cells may be increased by daily doses of 0.25 to 0.5 gm. per kilo of thyroid, but larger doses will not produce the same effect. The qualitative changes are always similar.

In the young individuals only were the red corpuscles, to a less degree, and the white, distinctly, raised. In the older rabbits the total blood counts showed no definite change except after prolonged feeding when a slight fall occurred. A marked relative polymorph increase was observed in the young rabbits, while in the adults this was transitory and less noticeable. When the polymorph percentage rises the mononuclear percentage falls, but even after prolonged feeding the latter does not rise. When a heavy dose of thyroid is given these changes are not so constant.

These observations suggest: (1) That the marrow is stimulated to activity, resulting in the increased production of polymorphs and small mononuclears, according to the age of the animal. The mononuclears do not reach the circulation as such, since there is never any obvious increase in the number of mononuclears after prolonged thyroid feeding. They must therefore undergo development into another type. (2) That increased production in the marrow should lead to an increase of the corpuscles in the circulation. This was not evident in the blood count, but might have been masked by some such factors as increased destruction of cells, an increased blood volume, etc. (3) That the marrow mononuclears are not responsible for the supply of mononuclears to the blood stream and therefore do not function as lymphocytes.

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(1a—464)

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**Effects of Thyroid, Thyroxin and Other Iodin Compounds upon Acetonitril Tests.**

*Masataro Miura, J. Lab. & Clin. Med., 7:349, March, 1922.*

The protective action of the thyroid is not a function of the iodin content alone, for potassium iodid or di-iodotyrosin, given by mouth, does not protect mice from poisoning with acetonitril. Thyroids vary in their ability to afford resistance to acetonitril poisoning, the fetal glands being the least effective in this respect. Thyroxin, in very small doses, may be as potent as the most active thyroid. In large doses it not only lowers the resistance of the animal to acetonitril, but also causes a loss in weight. This variance in the thyroids is not due to the iodin content, nor to a species difference, for the beef thyroids used differed among themselves.

Experiments proved that when thyroxin was fed in one-third the amount of the most active thyroid preparation used, based upon the iodin content, the protection against acetonitril was greater than that afforded by thyroid. This would indicate that the A iodin in the thyroid (one-half of all the iodin, insoluble in acid, curing myxedema and cretinism, and from which thyroxin was isolated) is concerned in the production of resistance to acetonitril, and that the thyroxin obtained from this fraction contains a protective substance in high concentration.

The results of the experiments demonstrated: (1) Desiccated thyroid fed to mice protects them against poisoning with acetonitril. The thyroid seems to be efficient in proportion to the amount of iodin contained. (2) Potassium iodid and di-iodotyrosin gave no protection against acetonitril, no matter what quantity was used. (3) Thyroxin, when fed in such amounts that it furnished one-third of the iodin provided by the most active thyroid fed, afforded a higher degree of protection in some cases. Increasing the amount of the thyroxin decreased the protection against acetonitril and caused loss of weight on the part of the animals.

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## 1b. BIOLOGIC AND ORGANIC CHEMISTRY.

(1b—165)

(1b—165)

### Research in Chemistry as Related to Medicine.

*Russell H. Chittenden, J. A. M. A., 78:1273, April 29, 1922.*

The application of biochemistry is so far reaching, so broadly extended, that there seems almost no limit to the possibilities it offers for furnishing aid in the prevention and cure of disease. Chemistry offers aid in the understanding of normal and abnormal function as well as in treatment, and can often aid in prevention. We need a more intimate knowledge of the cell and of the intracellular changes characteristic of life—how the cell constituents react on one another under changed conditions. We need more definite knowledge regarding the nature and distribution of the vitamins in our daily food. We now know that digestion of protein foods is a breaking down of the molecules into their constituent amino-acids, and that out of these the body cells can select the appropriate groups to build up their own peculiar units. We should have fuller knowledge of the protective substances.

The right type of man should be encouraged to enter upon research not as a side issue, but as a life work. The young investigator should be encouraged to become independent and self-reliant. There must be adequate facilities in library and laboratory. Coöperation is called for in many cases in which chemists, physiologists, bacteriologists, clinicians and hospital interns can work together with a common end in view, not as a group of subordinates controlled by one mind, but each as a master in his own particular field. This should not entirely replace the lone investigator who frequently works at his best only when he holds in his own hands all the threads that enter into the woof. Medicine is rapidly changing from an art to a science, and chemistry is destined to play an important part.

(1b—166)

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**Age and the Process of Hysteresis.**

*Wladislav Ruzička, Časop. lék. česk., 61 : 234, Prague, April 8, 15, 1922.*

Cytologic observations show that living substances contain chiefly chromatin during the stage of development and more achromatic substance (glastin) as age advances. The latter is a relatively quiescent physiologic formation while the former is relatively active. From biophysical reactions of these substances it appears that the protoplasm gradually changes from a labile (highly dispersive) state to a stable (slightly soluble and less dispersive) state. The aging of a body might be attributed to this change. Stabilization of the biocolloids cannot be solely explained by accumulation of insoluble vital products, but it involves the living substance itself whose solubility is physically changed. In this, condensation also plays a part. It is clear that the condensation of the dispersion phase of the colloids finally leads to decrease in metabolism, as it constitutes a progressive mechanical hindrance. This seems to be the most important point in the explanation of aging. The condensation of the living substance in the course of life the author calls "protoplasmic hysteresis," and the processes he calls "hysteretic processes." Some of these are reversible, but others are irreversible and they have great significance in morphologic metabolism and biology, under normal and pathologic conditions.

Among the differences between molecular dispersoids and colloids is the physical peculiarity that the former remain unchanged during their entire existence so long as they are not influenced by chemical reactions. Colloids, however, undergo changes. Many colloidal solutions flocculate while standing for a shorter or longer time, no other factor but time being responsible. Flocculation is a temporal function and is a sign of aging and hysteresis. The latter then is that condition in which the metastable colloids become more stable, less dispersive, and condensed. The progressive condensation is accompanied by slowing of the diffusion velocity of the crystalloids. The elasticity of the aging colloids decreases, they become more compact and lose the property of absorbing water (dehydration). The mutual attraction of the particles of the dispersion phase leads to reduced internal friction, and increased surface energy results from condensation. But this is a secondary manifestation. The primary is the aggregation of the particles whose electric charge influences the stability of the irreversible colloids. A reduction in the charge causes an attraction of the particles and there is flocculation and later coagulation if the charge drops to the minimum. The iso-electric point is that point at which the number of ions of the opposite charge are balanced. If aging of the body depends on processes analogous to this hysteresis of the colloids, it must be demonstrated that flocculation of the biocolloids in the older cells and tissues is greater than in the younger forms. It is known that the diffusibility and elasticity in the young cells and tissues are greater than in the older, and the intumescibility is diminished with age and dehydration increases. It is only necessary to determine the degree of aggregation or condensation. This may be done by (1) determination of the solubility (this method gives uniform results but there are many difficulties and it is not always practicable);

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(2) determination of H-ion concentration; (3) determination of viscosity; (4) determination of the osmotic pressure; (5) electro-endosmosis and cataphoresis; (6) flocculation of the albumins at the iso-electric point. The author has worked out the latter method to determine the degree of flocculation and the degree of aggregation of the dispersion phase of the colloid solution. This is easy to perform, and tissues, organs, dried substances and juices may be used. All experiments showed that the older tissues and juices are nearer to the iso-electric point, and this reaction shows that hysteresis or progressive condensation affects the living tissues and that the dispersion becomes less with advancing age. This demonstration may solve many important biologic problems, such as the scheme of metabolism, regeneration, the identity of a physiologic condition, the question of growth, maturity, sexuality, muscular work, variability and heredity. It may also be of value in medicolegal and clinical observations.

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(1b—167)

(1b—167)

The Estimation of Small Amounts of Sugar by Bertrand's Method.

Irene Greiner, *Biochem. Ztschr.*, 128:274, Berlin, March 7, 1922.

Bertrand's is the most useful of the various methods for determining small amounts of sugar. Instead of a solution of Rochelle salt, carbonate and bicarbonate, 2 solutions were employed, one of which contained only sodium carbonate and sodium bicarbonate, and the other Rochelle salt and sodium hydroxid. The following solutions were employed: (1) copper solution (Bertrand) containing 40 gm. copper sulphate dissolved in 1 liter water; (2) the alkaline Rochelle salt solution (Bertrand) containing 150 gm. sodium hydroxid and 200 gm. Rochelle salt dissolved in 1 liter water; (3) 150 gm. sodium carbonate and 30 gm. sodium bicarbonate dissolved in 1 liter water; (4) the iron solution (Bertrand) containing 50 gm. ferric sulphate and 200 gm. concentrated sulphuric acid dissolved in 1 liter water; (5) a 0.02 N potassium permanganate solution.

To 10 c.c. of the solution to be tested was added 10 c.c. each of copper solution and carbonate solution, then 10 c.c. of the alkaline Rochelle salt solution; the mixture was warmed and filtered and the residue washed exactly in accordance with original directions. This procedure formed the basis of the following calculation of glucose from the estimated copper: 10 mg. sugar corresponds to 20.8 mg. copper; 9 mg. sugar to 18.7 mg. copper; 8 mg. sugar to 16.6 mg. copper; 7 mg. sugar to 14.6 mg. copper; 6 mg. sugar to 12.5 mg. copper; 5 mg. sugar to 10.5 mg. copper; 4 mg. sugar to 8.44 mg. copper; 3 mg. sugar to 6.39 mg. copper; 2 mg. sugar to 4.34 mg. copper; 1 mg. sugar to 2.29 mg. copper.

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(1b—168)

A Micromodification of the Method of Benedict for the Quantitative Determination of Reducing Sugar in the Urine.

Millard Smith, *J. Lab. & Clin. Med.*, 7:364, March, 1922.

The modification usually employed consists in the use of from (Sec. 1—Page 1067)

one-fifth to two-fifths of the original amount of Benedict's solution specified for a determination. The amount of carbonate is correspondingly reduced, but the original volume is retained by the addition of 15-20 c.c. distilled water. Titration is as usual, in a porcelain dish. This modification leads to a variable error of 15-30%, due to the disturbed alkalinity of the titrating solution caused by the dilution of the reagent with water. Even the use of the same amount of carbonate as in the original determination does not remedy the error. The buffer action of the citrate is evidently necessary for the proper reaction. Another difficulty is the precipitation of the red oxid of copper, which obscures the end-point. This is due to dilution of the potassium sulfocyanate and potassium ferrocyanide. There is no reason why correct results cannot be obtained if proportionate amounts of the reagents are used. The difficulty in the determination of very weak (0.2%) sugar findings in the urine has been overcome, the end-point being sharper and the time of the determination being reduced. This was obtained by the use of 1 c.c. original Benedict quantitative solution without the addition of water, but with proportional reduction of the carbonate. This was carried out in a special test-tube.

*Technic:*—First 10 c.c. Benedict solution are pipetted into a test-tube, and 0.2-0.7 gm. anhydrous sodium carbonate is added. A small dry pebble should be added. The mixture is heated to boiling, and the urine added from a Mohr pipet until reduction is complete, as evidenced by disappearance of the blue color. For rapid reduction of the reagent vigorous boiling must be resorted to. However, this is not necessary if sufficient time is given for the reduction before the addition of the urine. The best results are obtained if the solution is kept at the boiling point and the urine is added slowly. The tendency in the titration of sugar is to go beyond the end-point, because reduction does not take place as in the ordinary titration methods. Near the end-point the urine must be added slowly. If graduated pipets are used, no calculation is necessary. If a Folin 5 c.c. microburet for urine-sugar is employed instead (the more accurate method), the calculation is:  $0.02 \div \text{the number of cubic centimeters of urine equals the percentage of sugar in the urine.}$

The average error by this method is plus or minus 5%. The titration of urines containing less than 0.17% sugar is very unsatisfactory. The most constant results are obtained by adding a large pinch of talcum powder to the tube before boiling. Besides giving the correct values this method decreases the cost and the time of determination and increases the ease with which the end-point of the titration is read and the various operations performed.

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(1b—169)

The Occurrence of Pyroracemic Acid in Normal and Diabetic Urine.

Robert Fricke, *Hoppe-Seyler's, Ztschr. f. physiol. Chem.*, 119:39, Berlin, March 14, 1922.

Stepp and Feulgen demonstrated the presence of acetaldehyd in diabetic urine. As acetaldehyd is formed from pyroracemic acid in yeast fermentation by cleavage of carbon dioxid (Neuberg), it was  
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to be assumed that a determinable amount of this preliminary stage of acetaldehyd is present in diabetic urine. For the detection of pyroracemic acid the very resistant pyroracemic acid-phenylhydrazid was employed, which is insensitive to heat with alkaline and moderate acid reactions. Pyroracemic acid-phenylhydrazid is identified by the melting point 192°, by boiling with 10% alcoholic sulphuric acid, by possible conversion into acetyl ether of melting point 114-115°, and by reduction with sodium amalgam to phenylhydrazinpropionic acid, melting point 152°. For the detection 5 liters diabetic urine were heated with phenylhydrazin, allowed to stand several days and filtered from the precipitate. The latter was then extracted with 96% alcohol, the alcoholic extract freed from alcohol and the residue extracted with glacial acetic acid. Though no pyroracemic acid could be detected by these means, either in normal or diabetic urine, its absence is not proved thereby.

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(1b—170)

(1b—170)

**A Micro Method for the Estimation of Ammonia in Blood and in Organic Fluids.**

*K. L. Gad-Andresen, J. Biol. Chem., 51:367, April, 1922.*

A special evaporating apparatus is called for consisting of a glass tube 25 cm. x 10 mm. provided with a bulb in which the blood and borate are mixed. The air current, which is introduced at the other end through a small bent glass tube and rubber stopper, first passes through a wash bottle containing concentrated sulphuric acid, which not only frees it from ammonia but also dries it and thus greatly increases the rate at which the blood is evaporated. The other end of the evaporating apparatus, as illustrated, is drawn out into a narrow tube and bent so that it will dip under the surface of the sulphuric acid in the analysis bottle. During evaporation the apparatus is placed in a thermostat at about 25°. A temperature exceeding 30° must be avoided because urea is then converted into ammonia. A hypobromite solution of constant composition must be used, controlled, and corrected for by a Kjeldahl determination. In making the ammonia estimations on the blood 1 c.c. blood is placed in the bulb of the apparatus, into which has been previously put 0.1 c.c. borate (9 c.c. of borate plus 1 c.c. of NaOH). The stopper is inserted and the tube rotated so that blood and borax are thoroughly mixed. The apparatus is then tilted so that the blood flows towards the end of the tube where the air current enters. Care must be taken not to get any of the blood into the narrow connecting tube because when the air current is opened it may then be carried over into the acid and ruin the determination. The blood is distributed over the entire surface of the tube and the latter is then placed in the water bath and connected up with the bottle of the micro-respiration apparatus in which has been placed 0.5 c.c. of 0.2 NH<sub>2</sub>SO<sub>4</sub>. The air current is cautiously opened and regulated so as to prevent the possibility of the material splashing out of the bottle. Evaporation to dryness is complete in about thirty minutes and the ammonia is estimated in the usual way in the micro respiration apparatus. In order to facilitate the calculation of the evolved quantity of nitrogen it is to be noted that the same quantity of fluid is to be used in the analysis reservoir each time. This can be made so that the

reservoir is tared and then, when the analysis is finished, weighted up with distilled water to a certain amount (for instance, 2.5 gm.). This weighing must not differ at the utmost more than 0.10 gm. If care is taken that the volume of the analysis reservoir is not altered, the calculation of the analysis result is very simple, as the c.mm. of evolved nitrogen is multiplied by the proportion: 1.256 by 1.09 by  $10^2 \div V$  by  $10^6$ , in which  $V$  signifies the quantity of blood used for the determination. The results show an average error of 0.03 mg. per 100 c.c. Secretions as well as blood may be analyzed by this method, but not tissues.

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**A Micro Urease Method for the Estimation of Urea in Blood, Secretions and Tissues.**

*K. L. Gad-Andresen, J. Biol. Chem., 51:373, April, 1922.*

A previous article described a micro method for the estimation of ammonia in blood and in organic secretions. Utilizing the same principle, a micro urease method has been worked out for the estimation of urea in blood, tissues, and organic secretions. The procedure is exactly the same as that described under the ammonia method, except that in this case the urea is first converted into ammonia by means of urease anhydrid, after which borate is added and the blood evaporated to dryness. The same correction is applied to the nitrogen found as in the ammonia method (that is, multiplication by the factor 1.09), and the calculation of the results is the same. The procedure estimates at the same time the preformed ammonia, but as this is very small and almost constantly 0.25 mg. per 100 c.c. this figure may safely be used for subtraction to obtain the true urea value. The limit of error by this method is 0.5 mg. per 100 c.c.

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**A New Apparatus for the Determination of Urea.**

*Luigi Condorelli, Policlinico (Pract. Sect.), 29:454, Rome, April 3, 1922.*

This apparatus, simple and convenient, consists of a small phial with a wide neck of a diameter of 4-5 cm. and a length of 8-9 cm., closed by a polished glass stopper that fits perfectly, and provided with a small vertical tubule. The latter has a lateral opening, that can be closed with a stop-cock. It is connected by means of a rubber tube 20 cm. long with a pipette, graduated from 1-100 cm. The pipette is plunged in a glass cylinder full of distilled water. It is held in the position desired by a screw-clamp fixed to a support by means of another clamp and maintained at a constant level corresponding to the upper end of the pipette. The apparatus is completed by a tube 6 cm. long and 1 cm. in diameter, which can readily be introduced into the phial with a pair of forceps. Into the phial are poured 10 c.c. hypobromite. The operator then cautiously introduces the small tube, in which is 2 c.c. of a mixture of blood serum and trichloracetic acid (20%), filtered and perfectly clear. (The experiment can be performed even with 1 c.c. of the mixture; in that case, the values obtained must be doubled to calculate the urea per liter of blood.) If the tube is long (Sec. 1—Page 1070)

enough, it will remain supported against the wall of the test-tube, and its content will not come in contact with the hypobromite. The phial is now closed with the stopper, holding the lateral tubule open, and the pipette is accordingly raised or lowered until the fluid within reaches the point O.

Naturally the level of the fluid in the cylinder will always be lower than that within the pipette, because in the latter there is capillary attraction. One must note how much higher the level of the fluid in the pipette is than that in the cylinder; this is easily shown, because the pipette is graduated. If, for example, with the tubule open, and hence with perfect equilibrium between internal pressure of the apparatus and atmospheric pressure, when the level of the fluid within the pipette is equal to 0, it is 0.5 outside, this signifies that the power of capillary attraction of the pipette is such as to cause the fluid to mount 5 divisions of 1 cm. each. This must be borne in mind, because, when taking the reading, in order to reestablish exactly the equilibrium between internal and external pressure, the pipette must be raised in such manner that the fluid within shall be 5 points above the external level of the fluid.

When the pipette has been adjusted so that the fluid is at 0, the lateral opening is closed, and the phial is shaken so that the fluid contained in the tubule mixes with the hypobromite. When gas-bubbles are no longer seen forming, the pipette is raised enough so that the internal level of the fluid is just as much above the external level as has been already calculated; then the reading is taken. Even with this method, the necessary corrections must of course be made for temperature and pressure. In using the apparatus, certain points must be observed: (1) not to have currents of warm or cold air in the room, for the temperature must be uniform; (2) the cylinder in which the pipette is plunged must always be full of distilled water, which takes on the room temperature. From the volume of gas obtained, by means of a table arranged by Condorelli, the volume of urea per liter of blood is determined.

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(1b—173)

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**A Colorimetric Determination of the Amino-Acid Nitrogen in Normal Urine.**

*Otto Folin, J. Biol. Chem., 51:393, April, 1922.*

For the colorimetric determination of the amino-acid nitrogen in normal urine Folin uses the method described in the preceding paper for blood, first, however, removing the ammonia from the urine by means of permutit. The process is as follows: Dilute from 5 to 25 c.c. urine to a volume of 25 c.c. in a 50 c.c. Erlenmeyer flask. Add 2-3 gm. permutit and agitate continuously, but gently, for five minutes. Decant the supernatant urine into another 50 c.c. flask. Again add 2-3 gm. permutit, and shake as before for five minutes. By this double extraction with permutit every trace of ammonia is removed. Decant the supernatant urine into a flask or test-tube.

To test-tubes graduated at 25 c.c. add 1, 2, and 3 c.c., respectively, of a standard glycocoll solution in 0.1N hydrochloric acid plus 0.2% sodium benzoate. This standard solution should contain 0.1 mg. glycocoll nitrogen per cubic centimeter. To these tubes add 1, 2, and 3 c.c.,

respectively, of the special 1% sodium carbonate solution described in the preceding paper. (1 c.c. sodium carbonate for each cubic centimeter of 0.1N hydrochloric acid present). Dilute the contents of each test-tube to a volume of 10 c.c. Transfer 5 c.c. of the ammonia-free (usually diluted) urine to another test-tube graduated at 25 c.c. Add 1 c.c. 0.1N hydrochloric acid and 1 c.c. 1% sodium carbonate solution. Dilute to 10 c.c. Dissolve 250 mg. amino-acid reagent in 50 c.c. water, and add 5 c.c. of this solution to each standard and to the unknown urine. Mix and set in a dark place over night. The following day the standard and the known or unknowns are first acidified by the addition of 1 c.c. of the special 25% acetic acid-acetate solution. To each are then added 5 c.c. 4% sodium thiosulphate solution. The contents of all the tubes are diluted to a volume of 25 c.c. and, after mixing, the color of the unknown is read against that of the standard having most nearly the same intensity of color. For the calculation it is essential to know which standard is used, and the actual volume of undiluted urine taken for the determination.

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(1b—174)

**Acetaldehyd a Constituent of Normal Urine.**

*W. Stepp and R. Feulgen, Hoppe-Seyler's, Ztschr. f. physiol. Chem., 119:72, Berlin, March 14, 1922.*

Acetaldehyd was detected in diabetic human urine with certainty in the form of a dimedon combination. Experiments were therefore undertaken to determine whether it also occurs in normal human urine. With this object urine was collected under the fullest precautions and distilled strongly alkalized in steam. The combined distillates were enriched by distillation until a distillate measuring 25 c.c. was obtained. To this 0.1 gm. dimedon dissolved in 1 c.c. alcohol (96%) was added. After twenty-four hours a crystalline precipitate separated whose melting point was 138°-140° after repeated purification. The anhydrid of the aldehyd combination had a melting point of 173°-175°. In the normal human being 0.3 mg. acetaldehyd is contained in one liter.

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**A Colorimetric Method for the Determination of Homogentisic Acid in Urine.**

*A. P. Briggs, J. Biol. Chem., 51:453, April, 1922.*

In tests for homogentisic acid in an alkaptone urine, p-diphenol gave the same color with phosphomolybdic acid as hydrochinon. Subsequently the homogentisic acid was isolated, its color ratio to hydrochinon determined, and hydrochinon used as the standard in the quantitative determination of homogentisic acid. The solutions used in the method are: (1) phosphate solution containing 1%  $\text{KH}_2\text{PO}_4$ ; (2) molybdate solution containing 5% ammonium molybdate in 5N  $\text{H}_2\text{SO}_4$ ; and (3) hydrochinon standard containing 1 mg. hydrochinon per c.c. Of the alkaptone urine 1 or 2 c.c. are diluted to about 15 c.c. in a 25 c.c. volumetric flask, 2 c.c. of the molybdate solution and 2 c.c. of the phosphate solution are added, and the mixture diluted with water to the 25 c.c. mark. To another flask containing equal amounts of the

phosphate and molybdate solutions, an appropriate amount of hydrochinon standard is added and diluted with water up to the mark. The flasks are inverted a few times so that the contents are well mixed, and the comparison is made in the colorimeter after five minutes. The average of several comparisons gave the author 1 mg. hydrochinon equal to 0.79 mg. homogentisic acid.

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(1b—176)

**Colorimetric Methods for the Separate Determination of Tyrosin, Tryptophan and Cystin in Proteins.**

*Otto Folin and Joseph M. Looney, J. Biol. Chem., 51:421, April, 1922.*

From preliminary experiments the authors learned that to determine tyrosin in protein digestion mixtures containing tryptophan the latter must first be removed. The substantially quantitative removal of tryptophan can be accomplished by means of the mercuric sulphate reagent of Hopkins and Cole. Summarizing the results of 26 different preliminary experiments made to determine the conditions for the quantitative separation of 1 mg. tyrosin from 1 mg. tryptophan, the authors note: (a) if the acidity of the final solution represents less than 3.5% sulphuric acid there is danger of loss of tyrosin, due to its precipitation by (2%) mercuric sulphate. (b) The tryptophan is quantitatively precipitated within two hours by 2% mercuric sulphate, when the acidity lies between 3.5 and 7.5% sulphuric acid. The authors made a series of analyses of various mixtures of tyrosin and tryptophan. Standard solutions of these substances were made in 5% sulphuric acid, each solution containing 1 mg. amino-acid per cubic centimeter. By means of 5 c.c. burettes graduated in 0.02 c.c., definite amounts of the amino-acid solutions were measured into 15 c.c. centrifuge tubes which had been graduated at a volume of 10 c.c. Of the mercuric sulphate solution (containing 10% mercuric sulphate and 5% sulphuric acid) 2 c.c. were added and the mixture was at once diluted with 5% sulphuric acid to the 10 c.c. mark. A rubber stopper was inserted, the solution shaken vigorously, then allowed to stand for two hours and finally centrifuged. The clear supernatant liquid containing the tyrosin was poured into a clean dry test tube and set aside for tyrosin determination. The centrifuge containing the mercuric tryptophan sediment was then filled to the 10 c.c. mark with 5% sulphuric acid, its own rubber stopper was again inserted and the mixture was shaken. After removing the stopper and centrifuging, the supernatant liquid was carefully poured out and drained for half a minute.

For the subsequent colorimetric determinations of tyrosin and tryptophan the process is as follows: For tyrosin.—Transfer 5 c.c. (one-half) of the tyrosin-containing liquid to a 100 c.c. volumetric flask, and into another similar flask introduce 1 c.c. of the standard sulphuric acid tyrosin solution containing 1 mg. tyrosin. To the latter add also 1 c.c. acid mercuric sulphate solution and 3 c.c. 5% sulphuric acid. Then add to each flask about 30 c.c. water, 20 c.c. saturated sodium carbonate solution, and 4 c.c. 5% sodium cyanid solution, in the order named. Add 2 c.c. phenol reagent, mix, let stand for thirty minutes and make the color comparison in the usual manner, setting the standard

at 20 millimeters. Twenty times 2 divided by the reading of the unknown gives the tyrosin found, in milligrams. For tryptophan.—To the unknown mercury precipitate and to a similarly precipitated and centrifuged standard containing 1 mg. tryptophan, add 10 c.c. water, insert the rubber stopper, and shake to secure a uniform suspension. Within three minutes add 4 c.c. 5% sodium cyanid to each, insert the rubber stoppers, and mix. Complete solution occurs at once, whereas a fine, more or less gelatinous residue containing tryptophan is left undissolved if the preliminary shaking of the sediment is omitted. Rinse the standard and the unknown into 100 c.c. volumetric flasks, keeping the volumes approximately equal (50 c.c.). Add first 20 c.c. sodium carbonate and finally, with shaking, 2 c.c. of the phenol reagent. Let stand for thirty minutes, dilute to volume and make the color comparison. When the standard is set at 20 millimeters, 20 divided by the reading of the unknown in millimeters gives, in milligrams, the amount of tryptophan present.

The colorimetric determination of cystin is based on the use of the uric acid reagent of Folin and Denis, and since neither tryptophane, tyrosin, nor any other known amino-acid except cystin gives a reaction with this reagent, the process for the determination of cystin in amino-acid mixtures is very simple.

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#### The Synthesis of Nitrates by the Biochemical Oxidation of Ammonia.

E. Boullanger, *Ann. de l'Inst. Pasteur*, 36:305, Paris, April, 1922.

The plant consists of 9 chambers, constructed of stone or cement. Each chamber contains 3 superposed compartments, separated by an interval assuring excellent ventilation. The compartments are filled with charcoal, kaolin, or similar material, which serves to support the nitrifying bacteria. Carbonate and phosphate of lime are also provided to meet the needs of the bacteria. When the chambers are charged, 300 liters of water, per cubic meter, are passed through the charges for eight days, in order to remove acid and organic substances. A solution of ammonium sulphate, 2.2 gm. to the liter, is then introduced and 40-80 liters per cubic meter of the charge are employed per 24 hours. Nitrification becomes fully developed in eighteen to thirty days. When active nitrifying bacteria are thus abundant, the ammonium sulphate solution is replaced by a solution of ammonium nitrate containing 0.45 gm. nitric nitrogen and 0.45 gm. ammoniacal nitrogen per liter. The latter solution is continually added for ten to fifteen days. Nitrification is regular and satisfactory, provided not more than 70 liters of the solution per cubic meter of the charge are used per day.

The oxidation of ammonia is nearly uniform in the several compartments. It should be allowed to occur slowly. Of the ammoniacal nitrogen 87 to 88% is transformed into nitrate. About 50 gm. nitric nitrogen may be produced per day, equivalent to about 286 gm. ammonium nitrate or 293 gm. calcium nitrate. A nitrifying bed of about 2 acres' surface and 1.80 thick, or about 18,000 cu. m., yields a little more than 5 tons of nitrate of ammonia or lime in twenty-four hours. This quantity is only about one-eighteenth of the return shown by the

tests in the laboratory of Müntz and Lainé. The industrial value is therefore much less than those tests would indicate. The charcoal does not give as good return as the clays, especially during the starting. During full action, the clays give slightly greater yields, but colorless and otherwise satisfactory solutions. The charcoals give a red and turbid liquid. The ammoniacal salt for the supply may be obtained from the liquid resulting from double decomposition of the nitrate of lime solution by ammonium sulphate or sesquicarbonate. The latter salt is preferable, because it provides continual regeneration of lime and seems to avoid the production of calcium sulphate, which clogs the compartments.

About 16 acres are needed for a suitable plant, of which 10 are required for the nitrifying beds, 1000 sq. m. for the building containing the receptacles, nitrified liquid and double decomposition, 8000 sq. m. for sheds, storehouses and the like, and 4 acres for laboratory, office and other space. The total capital required is about 5,000,000 francs. Wages will be about 600 francs a day, general expenses 600 francs a day. The total daily expense will be 2000 francs, the daily yield 10 tons ammonium nitrate, the cost per ton 200 francs.

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**Cow's Milk Casein.**

*B. Bleyer and R. Seidl, Biochem. Ztschr., 128:48, Berlin, March 7, 1922.*

The casein in milk is probably a casein and calcium combination which is strongly dispersive in water and forms colloidal solutions (or sols) as a result of which casein is separated either by hydrogen-ion action or by rennet. Analysis has shown only slight differences between acid and rennet casein, but experience indicates that acid casein possesses much greater capacity for reaction than rennet casein, so that a material difference between these substances must be assumed, which is not sufficiently explained by Hammarsten's cleavage theory. The different calcium caseinates contain fluctuating amounts of calcium oxide (0.3-2.9%). As a rule paracasein-lime (rennet casein) contains more calcium than does acid casein. By dissolving commercial acid casein in 0.01N lye, precipitating with 0.01N acetic acid, removing the fat and treating further by Pfyl's method, a pure product was obtained which was analyzed for ash content, nitrogen, phosphorus, sulphur and water. The average nitrogen content of acid casein was 15.5%, from which the nitrogen factor  $100 : 14.5 = 6.45$  is obtained. Paracasein similarly prepared contained 15.64% nitrogen. The final factor corresponding to this value is 6.39. In the determination of the equivalent weight of acid casein and paracasein as acid against 0.1N NaOH, KOH, NH<sub>4</sub>OH, Ca(OH)<sub>2</sub>, Sr(OH)<sub>2</sub> and Ba(OH)<sub>2</sub>, an average of 8.74 c.c. base was obtained, giving an equivalent weight for casein and paracasein as acids of 1145. The reaction isotherms between constant amounts of acid casein or paracasein and varying amounts of the lye gave values which showed that acid casein and paracasein react in the sense of Henry's law. The compounds of casein with alkaline earths, containing increasing amounts of oxides of alkaline earths are probably not true compounds but combinations in the sense of Henry's law. The so-called calcium caseinates containing calcium oxide

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in 0.3, 0.62, 0.8, 1.2, 1.5, 1.9, 2.3, 2.5 and 2.9% lie within the domain of Henry's solubility formula, having regard to experimental errors. The measurements of reaction isotherms between constant amounts of casein or paracasein and varying amounts of dilute acids (hydrochloric, sulphuric, lactic and acetic) gave the following results: (1) The formation of acid caseins or paracaseins is due to absorption. (2) The absorptive capacity of the two albuminoids is greatest in the case of hydrochloric acid, less with sulphuric and lactic and least with acetic acid. (3) Paracasein nearly always absorbs more acid than casein. On the whole, therefore, no particular difference exists between acid casein and paracasein in their relations to dilute acids.

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**Histopeptone.**

*K. Felix, Hoppe-Seyler's, Ztschr. f. physiol. Chem., 119:66, Berlin, March 14, 1922.*

Histopeptone is a peptone-like body formed from histon by digestion with peptohydrochloric acid. Kossel found it among the digestion products of histon derived from calf's thymus and determined its composition and properties. The present researches show that histopeptone derived from calf's thymus is a uniform body. Histon was obtained by straining freshly comminuted calf's thymus freed from fat, which was placed in an ice-chest together with toluol. From the nucleo-histon the histon was isolated by extraction with dilute sulphuric acid in the agitator, sulphated with ammonium sulphate and dialyzed until free from salt. The histon sulphate was digested ten days with peptohydrochloric acid at 37° and histopeptone isolated. Finally, histopeptone was prepared as sulphate and with the latter the estimation of hexone bases was carried out by Kossel and Kutscher's familiar method. The high proportion of lysin-nitrogen (13-16%) is noteworthy. Lysin-nitrogen, which is found from the amount of lysin picrate, is less than the total nitrogen according to Kjeldahl, but equal to the free amino-nitrogen of this fraction. Therefore, in addition to lysin, a substance containing no amino-nitrogen was precipitated by phosphotungstic acid. The estimations of hexone bases yielded values in general agreement with those found by Kossel. That the body is a uniform one appears also from the fact that no other bodies can be separated either by fractional sulphating or by precipitation with silver baryta at different H-ion concentrations. The quantitative digestion of histon showed that 30.1% of the total histon-nitrogen enters into the histopeptone.

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**The Proteins of the Tomato Seed, Solanum Esculentum.**

*Carl O. Johns and Charles E. F. Gersdorff, J. Biol. Chem., 51:439, April, 1922.*

The seed and press-cake used for these experiments were obtained from different sources. The meal for preparing proteins was made by grinding seeds of high germinating quality and removing most of the oil by extracting with ether. Analyses of 5 samples of tomato seed and press-cake showed an average content of 36.91% of protein ( $N \times 6.25$ ). The total globulins were extracted from the press-cake (Sec. 1—Page 1076)

with 0.5% sodium hydroxid. Preparations obtained from these extractions gave uniform results on analysis. From seed of high germinating quality 2 globulins,  $\alpha$  and  $\beta$  were isolated and analyzed. These globulins, coagulable by heating for ten minutes at 74° and 96° C., are precipitated from their saline solutions by 0.3 saturation in the case of the  $\alpha$  globulin, and by saturation with ammonium sulphate in the case of the  $\beta$  globulin. They differ in solubility, the  $\alpha$  globulin being easily denatured, while the  $\beta$  compound is highly soluble in mere traces of aqueous sodium chlorid. The sulphur content of the globulins is in the ratio 3:2. Analyses by the Van Slyke method showed that the nutritionally essential basic amino-acids are well represented in these globulins which are high in arginin and lysin, and respond to the qualitative tests for tryptophan and tyrosin. The  $\beta$  globulin was found to contain a large percentage of histidin, which was low in the  $\alpha$  globulin. Tests failed to disclose the presence of albumin and glutelin.

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**The Isolation of a Substance from Urine Having Properties of Citric Acid: Description of an Apparatus Facilitating the Working with Small Volumes of Gas.**

*Samuel Amberg and Mary E. Mayer, Am. J. Physiol., 60:564, May 1, 1922.*

By means of a very detailed method as well as a special form of gas apparatus (illustrated and described) the authors have isolated from urine in the form of an impure barium compound a substance which had the following properties in common with citric acid: (1) It gave the pentabromacetone and the typical Denigès reactions; (2) It yielded pentabromacetone and carbon monoxid in amounts closely equivalent; (3) It did not char on heating with concentrated sulphuric acid; (4) It gave the Sabanin-Laskowsky reaction; (5) Precipitates obtained according to Denigès' method behaved very similarly to precipitates from citric acid. From these precipitates a dry ether residue could be obtained, the aqueous solution of which gave the characteristic color reaction for acetonedicarboxylic acid with ferric chlorid. These results support their belief that citric acid occurs in the urine of normal human beings. Absolute proof, however, will depend on the isolation of the acid or its salts in a form pure enough for identification.

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**The Unsaturated Fatty Acids of Egg Lecithin.**

*P. A. Levene and Ida P. Rolf, J. Biol. Chem., 51:507, April, 1922.*

From egg lecithin 3 unsaturated fatty acids were isolated, namely oleic, linolic, and arachidonic. Oleic acid was identified by its iodin number and by its hydrogenation product, stearic acid. Linolic acid was isolated in small quantities only and was identified as its tetrabromid. Arachidonic acid was identified by its octabromid and by its hydrogenation product, arachidic acid.

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**The Influence of Radiation on Lipolysis.**

*Ludwig Pincussen and J. L. Anagnosu, Biochem. Ztschr., 128:268.  
Berlin, March 7, 1922.*

The influence of light rays and of the related energies of Roentgen rays and electric waves on the lipolytic power of serum was investigated. Serum taken from the animal and then irradiated, and serum of irradiated animals was examined. According to Michaelis and Rona the increased surface tension of a monobutyryl tributyrin solution produced by lipolysis is to be regarded as an exact indicator for lipolysis. The method is as follows: By shaking a few drops of monobutyryl or tributyrin with water or with a suitable phosphate solution, a saturated ester solution is prepared which is freed from excess ester by filtering through a moistened filter. To a definite volume of butyryl solution, usually 0.5 c.c. of the serum to be tested is added and the surface tension determined stalagmometrically. With radiations from high candle power incandescent light the ester-cleaving capacity of the serum was decreased in all cases whether monobutyryl or tributyrin had been employed. The decrease was very pronounced with both substances upon the addition of sensitizing pigments and moderate upon the addition of 5 c.c. 2% sodium dichloranthracenedisulphate solution. Roentgenization, on the other hand, has no influence on their ester-cleaving capacity. Experiments on the influence of irradiation of the whole animal on the lipolytic capacity of its serum showed partly a similar picture, but partly considerable deviations, inasmuch as, in contradistinction to normal roentgenized serum, a distinct decrease took place in the lipolysis by the irradiated animal's serum, which continued to increase considerably several days subsequent to irradiation.

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**The Course of Alcoholic Fermentation in the Presence of Urea.**

*Marta Sandberg, Biochem. Ztschr., 128:76, Berlin, March 7, 1922.*

The equation for the conversion of sugar under the influence of substances with alkaline reaction, according to the third fermentation type, is as follows:  $2 C_6H_{12}O_6 + H_2O \rightleftharpoons CH_3COOH + C_2H_5OH + 2 C_3H_5O_3 + 2 CO_2$ . In this, acetaldehyd is increased transiently. Acetic acid and ethyl alcohol on the contrary are produced by dismutation of acetaldehyd, while in glycerin the reduction product is formed. It was proposed to grow yeast on liquid containing urea. As simultaneous production of alcohol takes place in the growing of yeast on sugar solution it seemed worth while to investigate the influence of increasing urea concentration on the fermentative process. It was shown that even the weak urea base diminishes alcohol yield. Acetic acid and glycerin were not estimated. In the actual fermentation practically no urea was consumed, the determinations being made by the method of Mörner and Sjöquist.

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**The Influence of Sodium Chlorid on Dextrose Mutarotation in Alkaline Solution.**

*Hans Murschhauser, Biochem. Ztschr., 128: 215, Berlin, March 7, 1922.*

The accelerated mutarotation of an aqueous dextrose solution produced by sodium carbonate increases in proportion to the concentration of the salt. Sodium chlorid acts arrestingly on rotation retrogression of aqueous dextrose solution. To retard the processes, as compared to its rapidity in a solution in distilled water, to the extent of 3.6 units a concentration of 4 mols sodium chlorid to the liter is required. An acceleration analogous to this retardation is however effected with only about  $\frac{N}{5700}$  sodium carbonate solution, as appears from calculated results. The authors investigated in what sense mutarotation of dextrose in sodium carbonate solution of definite concentration is affected by varying amounts of sodium chlorid and finally whether a true relation exists between the rapidity constant and sodium chlorid concentration. The sodium carbonate solution on which these experiments are based was to be approximately  $\frac{N}{2000}$ , and only the amount of sodium chlorid was to be variable. The researches show that mutarotation of dextrose in alkaline solution (about  $\frac{N}{2000}$   $\text{Na}_2\text{CO}_3$ ) is retarded by increasing amounts of sodium chlorid, the retardations being directly proportional to the cube root of the solution's sodium chlorid concentration. The influence of sodium chlorid on the rapidity of mutarotation in acid solution was also investigated and it was found that addition of sodium chlorid to the acid dextrose solution accelerates. On the whole it was found that hydrochloric acid and sodium carbonate accelerate dextrose mutarotation and that sodium chlorid in aqueous solution retards. Addition of sodium chlorid to hydrochloric acid solution (0.361% HCl) increases acceleration in direct proportion to salt concentration. Addition of sodium chlorid to soda alkaline solution ( $\frac{N}{2000}$ ) retards velocity proportionately to the cube root of the sodium chlorid concentration. If the solution's hydroxyl-ion concentration is doubled, retardation is doubled with equal addition of sodium chlorid.

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**The Influence of Sodium Chlorid on Dextrose Mutarotation in Alkaline Solution.**

*Hans Murschhauser, Biochem. Ztschr., 128:229, Berlin, March 7, 1922.*

The authors investigated the increased rapidity of mutarotation produced by addition of a definite amount of sodium chlorid to a dextrose solution containing tenth-normal hydrochloric acid when the acid concentration is altered. The sodium chlorid concentration was kept constant, while acid concentration varied in the first experimental series between 0.046, 0.089, 0.181, 0.244, 0.361, and 0.54%; in the second series between 0.046, 0.089, 0.181 and 0.361%. It was shown that sodium chlorid accelerates mutarotation of acid dextrose solution only when the hydrochloric acid concentration is greater than 0.089%. Below this concentration the sodium chlorid has a retarding influence on

the acid, as well as on the pure aqueous dextrose solution. In order to enable the difference in the action of acid on water and on solutions in 2N or 4N amounts of sodium chlorid to be determined, the quotient for the pure acid action was calculated and found at 48.5. The influence of hydrochloric acid on the course of dextrose mutarotation in sodium chlorid sloutions of definite concentration consists in an acceleration of the process progressing with increasing hydrochloric acid concentration. But the accelerating action produced by addition of increasing amounts of hydrochloric acid to the sodium chlorid solutions is much greater than in aqueous solutions. These relations are shown arithmetically by a comparison of the average quotients calculated for the different solutions. The quotient for the acid action is 48.5 in aqueous solution, 71.5 in the solution combined with twofold normal sodium chlorid and 95.0 in that combined with fourfold normal sodium chlorid. The accelerating action of hydrochloric acid as against water is nearly doubled by the presence of 4 mols sodium chlorid, and the addition of half the amount of sodium chlorid effects an increase in the action of hydrochloric acid amounting exactly to one-half that produced by 4 mols sodium chlorid. This rule is valid for all acid concentrations in the same manner. These determinations show an almost mathematically exact dependence of mutarotation rapidity on acid and salt concentration and demonstrate the influence of sodium chlorid on mutarotation, though the cause of this influence of the neutral salt has not been fathomed.

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**Thioglucose.**

*Fritz Wrede, Hoppe-Seyler's, Ztschr. f. physiol. Chem., 119:46, Berlin, March 14, 1922.*

In the cleavage of several glucosids containing sulphur, a cleavage product was isolated as a silver salt the analysis of which suggested the probability of a sugar containing sulphur. The presence of thioglucose was regarded as proving the constitution of the natural mustard-oil glucosids, the best known of which is sinigrin (potassium myronate). Attempts to obtain thioglucose by the transposition of bromacetic glucose and potassium sulphid yielded a thiodisaccharid. It was still easier to obtain a diglucosyldisulphid in the form of the acetate from bromacetic glucose and potassium disulphid. Both diglucosyl disulphid and its finely crystallized octo-acetate are reduced by nascent hydrogen in acid, neutral and alkaline solution. The course of reduction could be followed easily by the alteration of optical activity. The reduction product was acetylated with acetic anhydrid and sodium acetate and the beautiful crystalline pentacetyl thioglucose prepared. By reduction with good aluminum amalgam in acetic alcoholic solution, tetraacetyl thioglucose is obtained from the acetate of diglucosyl disulphid. In spite of the free SH-group this does not form a silver salt with ammoniacal silver nitrate in alcoholic solution. If an ethereal solution of diazomethane be allowed to act on the substance, a violent reaction takes place with evolution of nitrogen. From ethereal solutions the tetraacetate of  $\beta$ -thiomethyl glucosid crystallizes. The thio-derivative, the same as tetraacetyl glucose, showed mutarotation. Diglucosyl disulphid octo-acetate, was prepared by adding precipitated

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sulphur to alcoholic potassium sulphid and boiling the potassium disulphid solution so obtained with the calculated amount of bromacetic glucose. After allowing to stand on ice it was recrystallized from benzol. The yield was 6 gm. from 20 gm. bromacetic glucose. About 5 gm. of the diglucosyl disulphid acetate was boiled with 50 c.c. acetic anhydrid and 1 gm. anhydrous sodium acetate, 10 gm. zinc dust being added while the liquid continued to boil lightly. Pentacetate crystals separated and after recrystallizing with methyl alcohol the substance was obtained in the pure state. The pentacetate forms coarse, white needles with melting point 121° and reduces Fehling's solution only upon boiling. Indigocarmine solution rendered alkaline with soda is easily decolorized on boiling with pentacetate. From the octo-acetates of diglucosyl disulphid, tetraacetyl thioglucose is formed by reduction with good aluminum amalgam. This melts at 75°, is soluble in alcohol, ether, chloroform and benzol and shows mutarotation. Thioglucose is formed by reduction of diglucosyl disulphid in acetic 95% alcoholic solution with sodium or aluminum amalgams. It is a beautiful white powder, strongly hygroscopic and shows mutarotation. With dilute acids and lyes thioglucose is easily cleaved on boiling. For the preparation of the silver salt of thioglucose its pentacetate is saponified with methyl alcoholic ammonia, evaporated in vacuo, alcoholic ammoniacal silver oxid solution added as long as a precipitate forms and then siphoned off, washed with alcohol and dried in vacuo. The silver salt can be decomposed with methyl iodid.

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**The Adsorption of Ferments and Zymogens. I.**

*Martin Jacoby and T. Shimizu, Biochem. Ztschr., 128: 100, Berlin, March 7, 1922.*

The adsorption of ferments is of practical and preparative importance. Freshly prepared tribasic calcium phosphate was employed as adsorptive agent. In the urease examination 10 c.c. calcium phosphate suspension was mixed with 30 c.c. 0.3% urease solution and 1 c.c. toluol added. In a control the suspension was replaced by 10 c.c. water. Both samples remained nineteen hours in the ice-chest following which they were centrifuged, the residue added to 20 c.c. water and placed twenty-three hours in the incubator. Considerable adsorption was however obtainable only upon addition of electrolytes (sodium chlorid). Further experiments were conducted with urease-nickel zymogen, and urease-cobalt zymogen which showed unmistakably that zymogen is adsorbed as such. With the aid of potassium cyanid reactivation it was detectable in the residue. Dibasic calcium phosphate did not adsorb either urease or its artificial zymogens.

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**The Adsorption of Ferments and Zymogens. II. The Action of Cholesterol on Urease.**

*T. Shimizu, Biochem. Ztschr., 128:103, Berlin, March 7, 1922.*

In experiments to determine the adsorption of cholesterol to ferments 10 c.c. 3% soy urease solution was mixed with 1 c.c. 10% sodium (Sec. 1—Page 1081)

chlorid solution and 1 c.c. hot saturated alcoholic cholesterol solution was added. One sample was filtered and the residue on the filter as well as the filtrate examined. In a fourth sample filtrate and filter residue were subsequently reunited. The following values were obtained after incubating 19.5 hours; without separation 63.4; filtrate 21.8; precipitate 1.9; filtrate and precipitate 11.3. By the action of cholesterol, changes in the ferment or in its medium must therefore take place, which become active only when the undissolved has been separated from the dissolved portion by filtration. That the changes can not be reversed after mixing the separated portion, but that the undissolved portion even arrests the action of the active substances in the solution after mixing, is further proof of the supervention of a change due to separation by filtration. Artificial zymogen likewise yielded results. Together with 30 c.c. urease solution 1 gm. powdered nickel was placed twenty hours in an ice-chest and then carefully separated; 0.3 sodium chlorid was added and precipitation effected with 3 c.c. hot saturated alcoholic cholesterol solution. After an hour the liquid was filtered. To 2 samples of 10 c.c. each of the filtrate, 2 c.c. water was added and the samples prepared for the urease examination. Two other samples were diluted correspondingly, 0.05 gm. glycocoll being added to each. Two further samples received 0.002 gm. potassium cyanid. After forty-six hours in the incubator, these values were obtained: Filtrate only, 3.6 and 3.6; with glycocoll, 80.6 and 81.2, and with potassium cyanid, 86.0 and 86.7. Accordingly, the inactivity of zymogens is not interfered with by the cholesterol precipitation and they pass unaltered into the filtrate. This points to a certain stability of the metallic combinations. Experiments with glycocoll show that the former activity of the altered ferment medium is again restored by the substance which Jacoby has termed auxo-urease.

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**Artificial Zymogens.**

*Martin Jacoby, Biochem. Ztschr., 128:80, Berlin, March 7, 1922.*

Metallic compounds of ferments that can be reactivated are termed artificial zymogens. That nickel passes into the ferment solution, is demonstrable by Tschugaeff's test. In the experiments 1 gm. powdered nickel is mixed with 47 c.c. 3% urease solution and 0.5 c.c. toluol added; 2 gm. powdered nickel is mixed with 100 c.c. distilled water and 0.5 c.c. toluol. The mixtures remain twenty-four hours in the ice-chest. During this time they are frequently stirred, then centrifuged and filtered twice through paper. The samples were prepared so that every 2 c.c. of the solution to be tested should receive an addition of 0.5 c.c. ammonia and a small amount of solid dimethyldioxin. The limit of the maximum reaction lies at a dilution of 1:2.5 in a ferment solution. In water the liquid must be concentrated to 1/7.5 of its volume. The authors investigated the effect of leaving the ferment solutions in contact with nickel powder for different periods, in what way activity is altered thereby, and how long the nickel-ferment compound separated from the undissolved nickel powder may be kept without undergoing alteration. In the conversion of ferment into zymogens and of zymogens into ferment the experimental procedure in which undissolved

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metallic powder remains present must be distinguished from the procedure employing clear solutions. In the presence of metallic powder spontaneous reactivation never takes place and it is certain that the activity of ferment solutions alters with the duration of contact of ferment solution and nickel powder in such a manner that active ferment diminishes while zymogen increases. In the case of clear ferment solutions changes take place in both directions, i. e., active ferment decreases and zymogen increases, or conversely. Gradually zymogens become permanently irreversible, but besides this final condition earlier temporary irreversible conditions of zymogens exist in which activation by customary agents is not possible.

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**Artificial Zymogens. III. The Action of Metals Related to Nickel on Soy Urease.**

*Martin Jacoby and T. Shimizu, Biochem. Ztschr., 128:89, Berlin, March 7, 1922.*

In order to gain an insight into the reaction leading to the combination of urease with nickel, the elements in the same numerical series with nickel were compared. These include iron, cobalt, nickel, copper, and zinc. From the dried urease a 3% solution was prepared, and the opaque filtrate employed for the experiment. The ferment solution and the metals were kept in an ice-chest during the experimental period, then centrifuged and filtered twice. Toluol (0.5 c.c.) as an antiseptic and olive oil (0.3 c.c.) to prevent frothing were added. Whereas nickel, cobalt, copper and zinc inactivate urease, iron does not inactivate urease. Although the other substances examined inactivate urease, differences are nevertheless found. In the case of cobalt, copper and zinc inactivation takes place more rapidly than with nickel. With cobalt and copper the amount of active zymogen diminishes very rapidly with the duration of action. Zinc is particularly effective, even very small amounts inactivate urease. When zinc has acted for a considerable time on urease, reactivity is still recognizable. The property of the metals to form complex compounds with potassium cyanid or amino-acids presupposes that they combine with urease and other ferments to form zymogens.

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**Artificial Zymogens. IV. The Inactivation and Reactivation of Taka-Diastase.**

*T. Shimizu, Biochem. Ztschr., 128:95, Berlin, March 7, 1922.*

Jacoby's researches have made known the inactivation reactions of urease with a series of substances. Another ferment, namely diastase, was employed for comparative studies in this direction. Herein, an unmistakable difference in the reaction capacity was found to exist in addition to partial agreement. In the inactivation of sublimate complete parallelism between the 2 ferments was found while the metals of the nickel series showed very distinct differences. With sublimate it was possible to produce inactivation that could be reactivated by potassium cyanid, while taka-diastase is not inactivated by nickel, cobalt, copper and iron in the experimental procedure that yielded inactivation of soja-urease by nickel, cobalt and copper.

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**The Influence of Cobalt-Amins on the Fermentative Action of Catalase and Amylase.**

*Eberhard Funk, Biochem. Ztschr., 128:108, Berlin, March 7, 1922.*

The influence of complex salts on fermentative effects was investigated in a series differing radically only in the number of certain groups in complexes. Hexaminocobaltichlorid, nitropentaminocobaltichlorid, dinitrotetraminocobaltichlorid, trinitrotriaminocobaltate, potassium tetranitrodiaminocobaltate (Erdmann's salt) and sodium hexanitrocobaltate were employed. The salts of the cobaltamins arrest the fermentative action of catalase and promote that of amylase and in this process a regular spasmodic alteration of the arresting or retarding action was observed. In the experiments the individual members of the cobalt series were allowed to act on the fermentative action of catalase in 0.01, 0.001 and 0.0001 N mol aqueous dilutions. Catalase was obtained from blood. Increasing concentration of the salt solutions showed a material increase in the arresting action on the catalase action. The slightest amounts of the salts (0.01%, 0.001% and 0.0001%) gave distinctly visible arrest of catalase action. If the neutral reaction of the medium was assured by Sörensen phosphate mixture ( $\text{pH}=7.15-6.98$ ) the arresting action of the cobalt combinations was abolished. An exception to this is Erdmann's salt. Contrary to the action of amylase only a slight increased effect is obtained with increasing concentration of the solutions. The slightest amount of the salts which effect visible promotion in amylase are considerably larger than those acting arrestingly on catalase, namely 0.01 N dilutions of the salt solutions. In the influence on catalase an increase of the arresting action is demonstrable for the individual members of the series when arranged in a definite order. With decreasing electrolytic conductivity the arresting power rises.

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**The Influence of Different Cations, Anions and Electrolyte Mixtures on the Decomposition of Urea by Urease.**

*D. H. Wester, Biochem. Ztschr., 128:279, Berlin, March 7, 1922.*

Urease is capable of converting urea into ammonium carbonate. The latter may be estimated titrmetrically with acid and methyl orange as indicator, each cubic centimeter tenth-normal acid that combines corresponding to 3 mg. converted urea. Soy beans and jack beans were used as the enzyme source. The powdered seeds were macerated in a mixture of equal volumes of glycerin and water and filtered after twenty-four hours. This urease solution keeps well for a long time in clean, stoppered bottles; aqueous solutions must be freshly prepared. A measured number of cubic centimeters are mixed with a definite amount of fresh urea solution or with certain chemicals, filled to 100 c.c. and kept at constant temperature. At definite intervals 10 c.c. or 25 c.c. of the mixture are pipeted and filtered. The enzyme is injured by tannic acid, iodin and copper sulphate; sublimate 1:1,000,000 and thymol have little effect on it, while chloroform (if anything) promotes its activity. Methyl alcohol and ethyl alcohol influence urease action only slightly. Amyl alcohol and ether are slightly injurious. Sodium

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ion retards more than potassium ion, and calcium ion even more so. Addition of salts, such as calcium chlorid, seems to eliminate the action somewhat. Hydrogen sulphid is not poisonous to urease. The retarding action of cations rises regularly with the concentration and in the order  $K < Na < Ba < Mg$ . The action of anions is much less than that of cations.

Lithium retards more strongly than potassium. The action of a mixture of potassium sulphate and lithium sulphate is a diminishing one. The retarding action of a mixture of potassium sulphate and sodium chlorid and of one of magnesium sulphate and potassium sulphate is almost the same as that of the most poisonous component. The influence of ammonium chlorid is peculiar. By itself it promotes the urealytic activity of urease only slightly, but in combination with potassium sulphate, magnesium sulphate or a mixture of these salts with sodium chlorid it exhibits very strong poison removing properties. The experiments always yielded analogous results with urease derived from different sources, with aqueous and glycerin-water mediums, under different temperatures and with salts of different concentrations.

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(1b—195)

**A Special Action of Urease Ferment on the Animal Organism.**

*Alfred Lublin, Arch. f. exper. Path. u. Pharmakol., 92:280, Leipzig, March 10, 1922.*

Having convinced himself of the usefulness, for the estimation of urea, of the ferment urease, found in the soy bean, jack bean, root of pseudo-acacia and in a number of other plants, Lublin also confirmed the fact that the urea values obtained by it in urine, blood, transudates and exudates, agree with those obtained by Bang's micro-determination. He thereupon proceeded to investigate the action of urease on the animal organism. Large doses of urease were injected subcutaneously into white mice, which succumbed after twenty-four hours under signs of ammonia poisoning. In rabbits, subcutaneous injection of urease does not cause death nor does it diminish blood-urea, but following intravenous injection of small amounts of urease the animals died in as short a time as forty-five minutes. They showed the embolism picture, which is probably due to agglutination of erythrocytes by even small amounts of urease. In one instance Lublin observed hemoglobinuria in a rabbit following urease injection. If, however, blood-urea be increased in the rabbit by parenteral administration of urea, the animals die of ammonia poisoning even following subcutaneous urease injection.

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(1b—196)

(1b—196)

**Improved Method for the Preparation of Vitamin-Activated Fuller's Earth.**

*Atherton Seidell, Pub. Health Rep. (U. S. P. H. S.), 37:801, April 7, 1922.*

Formerly vitamin-activated fuller's earth was prepared by allowing fresh yeast to autolyze and filtering the resulting product to which clear liquid fuller's earth was added and thoroughly agitated, after which the  
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solid was removed by filtration, washed and dried. The most unsatisfactory step in this process was the extremely slow and wasteful filtration of the autolyzed yeast. After more or less unsuccessful experimentation to eliminate this trouble advantage was taken of the observation that when fresh yeast is added to boiling water acidified with 0.01% acetic acid the yeast cells are disrupted, the protein is coagulated and the vitamin is set free to enter the aqueous solution which can readily be separated from the coagulated protein and insoluble material. It is a much more satisfactory solution for the adsorption of vitamin by fuller's earth and the very complex filtrate from autolyzed yeast. In addition to shortening and simplifying the process it also offers the great advantage of being practically free from adenin, one of the interfering substances simultaneously adsorbed with the vitamin. Samples of activated solid prepared by this process contain but 1.5% N as compared with 2% by the old method. The content of antineuritic vitamin as estimated by feeding experiments on pigeons was found to be about twice as great as that of the product made by the original method.

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### 1c. PHARMACOLOGY AND TOXICOLOGY.

(1c—205)

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#### Preliminary Tests of Unknown Drugs. Narcotics.

*John Grönberg, Acta med. scandin., 56:230, no. 3, Stockholm.  
1922.*

This article constitutes a plea for the biologic testing of all new drugs, especially narcotics, before their introduction into the pharmaceutical trade. If such a procedure became general, many untoward sequels and poisonings from narcotics and hypnotics would be avoided. For practical purposes, the method of analysis must be as simple as possible without detracting from the reliability of the results or overlooking important actions. It should be understood that many supposedly new compounds are merely combinations of familiar substances, and these can usually be compared with known drugs. In testing new preparations, the minimum effective, minimum injurious and minimum lethal doses must be determined. The general properties should first be learned and the test animal (usually frogs and rabbits) selected; the breed and feeding of the animal may be an important element in the tests. Studies with frogs should be scrutinized with special care, and only *Rana temporaria* weighing about 30 gm. should be employed. The rabbits should weigh about 1 kg. The desirable working dose may be arrived at by trying out 1 and 5 mg., 1 and 5 cg. and 1 and 5 dg. on frogs, or proportionately larger doses on rabbits. The effects must be carefully observed and accurately recorded. The season is often an important factor as the physical condition of many animals varies greatly with the season. Thus lethal doses in frogs vary considerably with the period of the year.

To illustrate a standard procedure the author reports detailed tests with narcotics and hypnotics, including codein (phosphate), papaverin (hydrochlorid) pantopon, veronal, medinal, nirvanol and adalin (brom-diethyl acetyl urea). Some of these are constituents of many "new" (Sec. 1—Page 1086)

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drugs, and all are used extensively in general practice. The following table summarizes the results of the pharmacologic tests with these drugs on tadpoles (10-14 mm. long), frogs (30 gm.) and rabbits (1 kg.). The doses for man are based on the results obtained by other investigators, reports from the literature, or computations based on animal or clinical findings with the same or comparable agents. All doses are given in fractions of 1 gm., except for tadpoles, for which they are indicated by percentage.

Drug	Genus	Minimum effective dose	Minimum injurious dose	Minimum lethal dose
Codein phosph.	Frog	0.004	0.005	0.01
	Rabbit	0.04	0.06	0.1
	Man	0.03	0.1	
Papaverin hydrochlor.	Frog	0.0005	0.001	0.002
	Rabbit	0.1	1.	1.8
	Man	0.03		
Pantopon	Frog		0.0025	0.001
	Rabbit	0.01	0.05	0.2
	Man	0.02	0.06	0.2
Veronal	Tadpole	0.6%		0.8%
	Frog	0.0054	0.18	0.045
	Rabbit	0.01	0.2	0.4
	Man	0.5	0.75	5-10
Nirvanol	Tadpole	0.05%		0.07%
	Frog	0.0015	0.002	0.005
	Rabbit	0.15	0.2	0.2
	Man	0.5		
Adalin	Tadpole	0.02%		0.03%
	Frog	0.01	0.025	0.05
	Rabbit		0.25	0.6
	Man	0.75-1.		

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**Pharmacologic Studies on Acetone.**

*William Salant and Nathaniel Kleitman, J. Pharmacol. & Exper. Ther., 19:293, May, 1922.*

The influence of acetone on the circulation and respiration was studied in cats and dogs. Even moderate amounts injected intravenously caused a very considerable fall in the blood pressure, the diminution in the volume of the kidney which accompanied it showing that the depression of the circulation was stimulated by small doses of acetone, larger doses always causing depression. Speed of injection and repetition of dose were important factors in determining its action. The effect was more marked and more prolonged in cats than in dogs, which may be accounted for by the different speeds of elimination in these animals. Acetone was still present in the blood of cats twenty-four hours after its administration, but it disappeared much sooner from the circulation in dogs. Narcosis and paralysis observed in experiments on frogs, cats and dogs showed that acetone also depresses the central nervous system. The centers in the medulla were variously affected, those of inhibition and vomiting being stimulated, while the respiratory center was stimulated by small and depressed by large doses. The influence of acetone on the isolated heart of the frog and the  
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turtle varied with the concentration, depression being much greater when the heart was perfused with 10 than with 5% acetone, while a solution of 1% failed to cause any effect even when the perfusion time was quite long. The change consisted in decreased force without noticeable alteration in the frequency of the heart beat, although in some cases slowing was observed. In all experiments recovery occurred when acetone solution was followed by perfusion with Ringer's solution alone. The effect on the heart of the turtle was less pronounced than on that of the frog.

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**Reversed Action of Adrenalin on the Surviving Uterus by  
Displacing of the Ions.**

*Max Turolt, Arch. f. Gynäk., 115:600, Berlin, Feb. 16, 1922.*

Turolt investigated whether the proportion of calcium ions and of potassium ions has a determining significance for the varying reaction of the uterus as regards adrenalin in pregnant and nonpregnant states and in different animals. Displacing of the ions was produced, by adding calcium or potassium in solution (1:1000) to the medium or by using Ringer's solution without calcium or potassium.

In normal nutritive solution, adrenalin produces a resting state of both the pregnant and nonpregnant uterus in guinea-pigs, but when there is an excess of calcium salts, adrenalin produces in both cases an excitation of the uterus. Potassium salts do not influence the action of adrenalin. On the contrary, in the human uterus, which is excited by suprarenal preparations in pregnant as well as in nonpregnant states, calcium salts produce an arrest of automatism and potassium salts produce a powerful excitation. The inhibiting excess in calcium salts can hinder the action of adrenalin only in the nonpregnant uterus; in the pregnant uterus, the adrenalin excitation persists in spite of calcium.

The differing reactions of the uteri in animal species must therefore be assigned to the varying content as regards physiologically active cations. The reversed action of adrenalin in the uterus of guinea-pig and of woman, after preparatory treatment by calcium, as well as the reversed action of adrenalin on the pregnant human uterus after preparatory treatment by potassium, shows that the modification of the cations content also is very important for the uterus as regards its varying susceptibility to poisons. It is probable that the contradictory observations of different investigators in the study of the action of adrenalin on surviving organs has been dependent upon the different salt contents of the organs. But the fact that the same cations influence in a reversed manner the uterus of guinea-pigs and of women in pregnant and nonpregnant states, must make us careful not to consider the displacing of cations as the sole cause of the modified reaction. Pregnancy may produce changes in the metabolism, chiefly in glands with internal secretion and these changes may be capable of abnormally modifying the action of cations and also of certain pharmaceutic products.

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**Successive Stimulation by Alcohols.**

*Marian Irwin, Am. J. Physiol., 60:274, April 1, 1922.*

In the author's experiments a series of monohydric saturated alcohols was used for a repeated stimulation of worms at different concentrations. The alcohols studied were methyl, ethyl, n-butyl, and is-amyl alcohol. In the case of each alcohol it was found that there is a certain concentration at which successive exposures bring about a decrease in the sensitivity of the worm; concentrations somewhat lower than this bring about an increase in sensitivity, and concentrations still lower cause no change. These facts may be accounted for by supposing that the alcohol, A, unites with a substance, X, in the prostomium of the worm to form a compound AX, which is necessary for stimulation. No stimulation can occur until this compound reaches a definite concentration. It is also obvious that this compound tends to disappear, since otherwise the weakest concentrations of alcohol would stimulate in the course of time, which is not the case. The rate of formation of AX depends on the concentration of both A and X and it is therefore evident that as the substance X is used up the reaction time must lengthen. If the concentration of alcohol is high enough, X is used up so rapidly that the reaction time begins to lengthen after a few exposures have been made. If there is a sufficiently long interval between exposures, X is more or less completely restored and a corresponding recovery of sensitivity will take place.

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**The Effect of Some Polyhydric Alcohols on the Behavior of Rats in the Circular Maze.**

*David I. Macht and Gu Ching Ting, Am. J. Physiol., 60:496, May 1, 1922.*

Albino rats were trained to solve the maze problem so as to find their way through labyrinthian paths to the center of the maze without committing any errors and in the shortest possible time. After the period of training various polyhydric alcohols were administered intraperitoneally and the behavior as well as somatic changes were noted at various intervals. Alcohols studied were ethylen, glycol, glycerol, erythrone, arabite, mannite, dulcite, perseite and volemite. The drugs were dissolved in water, in concentrations of from 1 to 3 5%. The object of the experiments was to determine the smallest quantity of the drugs used which produced a depression in the behavior of the rats. It is evident from the tabulated results that all of the substances examined produced a depression of the neuromuscular system and are narcotic in the broad sense of the word.

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**Sensory Stimulation by Unsaturated Alcohols, Polyhydric Alcohols and Chlorhydrins.**

*Marian Irwin, Am. J. Physiol., 60:270, April 1, 1922.*

The author tested the efficiency of such alcohols as allyl alcohol,  
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ethylene glycol, glycerol and of the chlorhydrins, ethlene chlorhydrin and glycerol chlorhydrin, by noting their effect on the sensory cells of *Allolobophora foetida*. These results were then compared with the effects of monohydric alcohols studied in a previous investigation. The method used was that previously employed by the author. When a worm is placed on a table, surrounded by a test solution, the worm will slowly crawl to the edge of the table and enter the solution. The time elapsing from the moment the prostomium enters the solution until it is withdrawn is the reaction time of the worm to the test solution. The author's tabulated results show that the efficiency of allyl alcohol is much greater than that of either glycol or glycerol. Glycerol monochlorhydrin was found less efficient than ethylene chlorhydrin. As for the narcotic effect of the reagents, allyl alcohol and chlorhydrins proved to be more efficient than glycerol and glycol.

(1c-211)

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**The Action of Cyanamid. II.**

Erich Hesse, *Ztschr. f. d. ges. exper. Med.*, 26:337, Berlin, March 6, 1922.

Cyanamid is capable of raising pharmacologic effects to the highest power. Experiments with quinin on the frog's heart, with cocaine on frog's nerve preparations and with curare on the whole frog gave negative results, nor could the action of nicotin on the frog's heart be increased by cyanamid. On the other hand the temperature-reducing action of chloroform in the rabbit (0.1 gm. cyanamid per kg. animal and after half an hour 40 c. c. chloroform—Ringer solution per 1.5 kg. orally) was increased by cyanamid. Furthermore, cyanamid destroys the action of atropin on the rabbit's vagus, i. e. after intravenous cyanamid administration, faradization of the vagus does not lower blood pressure. But the antagonist muscarin-atropin exists also in the cyanamidized animal. The combination of camphor and cyanamid shows no increase of the camphor action (spasms) in the rabbit. On the other hand subdoses of strychnin and picrotoxin combined with inactive cyanamid doses produce spasms. These experiments were carried out on *Rana esculenta*. The synthesis of amylenhydrate-glycuronic acid could not be influenced by cyanamid as was shown in urine examinations, by polarization in the rabbit. But in the application of phenol or chloral hydrate, with or without combination with cyanamid, the urine gave different rotation values. The differences amounted to 50%. The chloral hydrate was estimated by Tomasczewiz's method.

In formulating a theory of the cyanamid action Hesse proceeded from the assumption that cyanamid brings about better conditions for the solution of the active substances in the central nervous system. Thus it would act on distribution. In the case of bromin (estimated by Deniger's method) it was found that the brain of animals treated simultaneously with cyanamid contain more bromin than those that had received the same amounts of bromin only. The same was found for alcohol which can be estimated in the brain by reason of its oxidability by sulphuric potassium bichromate. As the activation of inactive theobromin doses was successfully accomplished in the rabbit by means of cyanamid, Hesse estimated the alkaloid in the urine by Wach-

tel's method, and increased secretion was observed after administration of cyanamid. In the examination of several derivates—dimethylcyanamid, diethylcyanamid, diamylcyanamid and phenylmethylcyanamid—uniform reactions in the animal experiment were not obtained. They produced sudden fall of temperature, narcosis or spasms.

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**Ergot of Oats and Ergot of a North African Grass.**

*G. Tanret, Bull. d. sc. pharmacol., 29:169, Paris, April, 1922.*

The ergot of rye has received most attention. Tanret examines ergot of oats and ergot of diss, a wild grass of North Africa, *Ampelodesmos tenax*. The ergot of these 2 plants contains the same active principles that occur in the ergot of rye. Their proportion varies considerably. The ergot of the grass is poor in ergotinin, while that of oats contains more than most specimens of rye ergot. The ergot of oats may be satisfactorily used instead of rye ergot under any and all circumstances. The ergot of the grass should be used only during emergencies, where rye ergot is lacking on account of droughts. The oat ergot should constitute an important commercial asset to North Africa, especially the Algerian provinces.

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**Variations of Oxymethylantraquinone Compounds in Frangula and Its Galenical Preparations.**

*E. Maurin, Bull. d. sc. pharmacol., 29:175, Paris, April, 1922.*

The variations in the oxymethylantraquinone compounds present in *Rhamnus frangula*, or the alder buckthorn, have been examined with reference to origin, age of the plant, drying period after gathering, and method of preparation. The geographic origin is not important, causing but little variation. The bark should be taken from plants 3 or 4 years old. The compounds are not fully formed in young plants, and diminish after the third or fourth year. It is preferable to use the plants soon after gathering. They deteriorate, and the therapeutic compounds diminish, after harvesting. The teaching that the plants should be dried for a year is a mistake. The fluid extract is the most effective form of preparation. The tincture is inferior, since extremely large quantities are required. The decoction is rather better than the infusion. The powder is better than the galenicals. The French plants are equal, or superior, to those of foreign growth.

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**Hyoscyamin and Its Sulphate.**

*A. Goris and P. Costy, Bull. d. sc. pharmacol., 29:113, Paris, March, 1922.*

To diminish the action of heat in the preparation of the extract of belladonna, and thus to lessen the danger of the hyoscyamin being transformed into atropin, the following experiments were undertaken to determine the effect of heat under different conditions on hyoscy-

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amin and its sulphate: (1) The preparation of pure hyoscyamin by separation of hyoscyamin from atropin, the method being based on the difference of solubility of hyoscyamin and atropin in hot and in cold benzene. (2) The preparation of the sulphate of hyoscyamin by the addition of sulphuric acid to pure hyoscyamin, and also the separation of this salt from the sulphate of atropin in a mixture of the two by washing the mixture in cold absolute alcohol or by dissolving it while warm in absolute alcohol and allowing it to crystallize by cooling, the result depending on the difference of solubility of the 2 salts in absolute alcohol. (3) The determination of the action of a incubator temperature of 100° C. on crystallized hyoscyamin. (4) The determination of the action of heat on hyoscyamin in an alcoholic and in an aqueous solution. (5) The determination of the action of a temperature of 100°C. on an aqueous solution of the sulphate of hyoscyamin.

Results indicated that hyoscyamin is fairly stable. Its polarity is not affected as readily as might be supposed. Aqueous solutions of the sulphate are stable at 100° C. if contained in neutral glasses. However, if physical changes are produced by chloroform or water, hyoscyamin is entirely changed to its isomer at 100° C. Transformation normally begins at 106° C. and total transformation is rapidly produced by 118° C.

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**Pharmacologic Researches on the Respiration Center. II. The Influence of Lobelin and Two Other Lobelia Alkaloids on the Narcotized or Morphinized Respiration Center. The Action of Lobelin on the Circulation.**

*Hermann Wieland and Rudolf Mayer, Arch. f. exper. Path. u. Pharmakol., 92:195, Leipsic, March 10, 1922.*

The authors examined 3 well-characterized substances from the lobelia alkaloids: (1) lobelin;  $C_{28}H_{29}O_2N$ , a unibasal acid with melting point 130° C., which splits off acetophenone on heating with water; (2) lobelidin,  $C_{29}H_{25}O_2N$  which also splits off acetophenone, (3) base B— $C_{22}H_{27}O_2N$  (?), the melting point of the free base being 99° C. The aqueous solutions of the hydrochlorates of these substances were examined. The height of the curve for the respiration center, expressed by the respiration-volume per minute, served to measure the action of lobelin. The respiration volume was measured by Gildemeister's gasometer which was connected with one end of a T-tube tied in the trachea of the experimental animal (rabbit). The poisons are injected into the jugular veins. The results show that lobelin increases irritability of the respiration center when the latter is narcotized by urethan, chloral hydrate and morphin. The smallest doses of lobelin suffice (0.5 mg. per kg. living weight) in morphin poisoning, larger doses are required than in poisoning by urethan (0.5 to 2.0 mg); and the largest doses in the case of chloral hydrate (1.0 to 4.0 mg). Considerable doses of lobelin first produce paralysis of respiration, becoming apparent by diminishing minute-respiration volume, and finally arrest of respiration. The effective dose obviously depends, not only on the quantity, but also on the rapidity of administration of the poison. A central vagus stimulation (atropin and vagus division experiments) and bronchoconstriction participate in the para-

lysis of respiration which is to be referred to a direct action on the musculature, as demonstrated by experiments on Trendelenburg's bronchial muscle. Lobelidin and base B possess the same action, though this is quantitatively weaker. All 3 substances act on the circulation, lowering blood pressure and frequently slowing the pulse, especially in large doses, an action due probably to their obviating cardiac asphyxia, owing to improved ventilation. Here, too, vagus stimulation plays a part by a central effect. In excised frogs' and rabbits' hearts the musculature is found to be influenced directly, without vagus action, up to arrest of the heart's action, with a lobelin concentration of 1 to 10,000. In addition, spasms of the musculature are induced by lobelin by central stimulation. Of therapeutic importance is the protracted influence on the respiration center which is attained especially by subcutaneous, and eventually by intramuscular, injection of the pharmaceutical agent. Blood pressure is not influenced by subcutaneous injection. Intravenous injection need be considered only when rapid recovery of irritability of the respiration center is desired.

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**Some Observations on the Action of Mercury.**

*William Salant and Nathaniel Kleitman, J. Pharmacol. & Exper. Ther., 19:315, May, 1922.*

The intravenous injection of the acetate, succinate and benzoate of mercury into cats, dogs and rabbits produced a sudden fall in blood pressure which was very marked and persistent. Depression and later paralysis of respiration also occurred. Cardiac inhibition was produced by the intravenous injection of the salts of mercury in cats, but not in dogs or rabbits. Decreased irritability of the vagus was observed in cats after the intravenous injection of the organic salts of mercury. That the fall in blood pressure after injection of mercury was of cardiac origin was shown by observations on changes in the volume of the kidney. Perfusion of the turtle heart with the different salts of mercury produced cardiac depression, irregularity and delirium cordis. Concentrations of 1 part of mercury to 1,000,000 parts of Ringer's solution, and even 1 to 10,000,000, were effective. The frog heart was more resistant to mercury than the turtle heart. No delirium cordis was observed. The action of mercury was cumulative.

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**Sodium Persulphate in the Analysis of Phosphorus Compounds.**

*L. Débourdeaux, Bull. d. sc. pharmacol., 29:89, Paris, Feb., 1922.*

This article concludes Débourdeaux's discussion. The application of sodium persulphate to analyses of hypophosphites, glycerophosphates, thymimates and nucleinates, is illustrated. Lecithin is insoluble in alkaline or acid aqueous media. On account of this fact, carbon cannot as yet be determined by the persulphate method. However, if treated by fuming nitric acid, a residue soluble in water or soda solution may be obtained. The residue is oxidizable by the general alkaline-acid process. Fatty substances present in the lecithin do not (Sec. 1—Page 1093)

embarrass the determination. At the end of the process, phosphoric acid is determined as triargentic phosphate, according to the method described.

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**Reactions of Nitric Acid with Phenols and Di-Ethers of Pyrocatechin and Homopyrocatechin.**

*R. Huerre, Bull. d. sc. pharmacol., 29:180, Paris, April, 1922.*

Huerre has studied the relations of the wood of juniper to the production of oil of cade, endeavoring to devise a test for small quantities of guaiacol, cresol, etc., in products derived from the heated wood. Guaiacol and its homologues give characteristic color reactions with nitric acid. With the di-ethers of pyrocatechin and homopyrocatechin, nitric acid yields crystalline nitrated compounds which permit the detection of very small quantities of guaiacol and cresol, when there is not enough pyroligneous oil to permit preparation of pure phenols. With guaiacol, the color is intense red. With cresol and eugenol it is orange, passing to red with an excess of nitric acid. Naphthol yields a brown, changing to violet in twenty-four hours. With thymol, no immediate color occurs, the solution becoming green in twenty-four hours. Pyrogallic acid becomes slightly greenish in twenty-four hours. Phenol becomes slightly yellowish in a minute, changing to orange. The test is negative with eucalyptol, resorcin, phloroglucin, salicylic acid, naphthol salicylate, and phenol salicylate. For the color tests, pure 36° C. nitric acid is added to the solution containing all quantities, up to and including saturation. The crystalline compounds must be differentiated by means of their solubilities, melting-points and the like. Beechwood creosote, distilling at 205° to 220° C. was treated with a solution of potash in methyl alcohol, then heated with methyl iodid at 150°. The dimethyl ethers thus obtained crystallize rapidly with nitric acid. Oil of cade was treated with a watery potash solution. The product was exhausted with ether, and HCl was added in excess. The impure phenols were treated with water vapor. The liquids carried off were treated with methyl potash and heated with methyl iodid at 150°. KI was eliminated, and crystallization produced with nitric acid.

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(1c—219)

**The Union of Quinin with Erythrocytes and the Action of Quinin on Cellular Respiration.**

*P. Rona and E. Bloch, Biochem. Ztschr., 128:161, Berlin, March 7, 1922.*

The toxic action of quinin on paramecium depends on the amount of free base contained in the solution as related to the permeability of the cells. On the other hand the union of quinin with erythrocytes is independent of the hydrogen-ion concentration and the blood-corpuscles are equally permeable to quinin salt and quinin base. This was investigated with sheep blood-corpuscles and with the nucleated red corpuscles of birdblood. The principle of the method is based on the fact that quinin poisons serum-lipase according to a definite law, from which it is possible to estimate the amount of quinin absorbed by

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blood-corpuses, when the decrease in the toxicity of a quinin solution to which red blood-corpuses have been added, and which has been recovered by centrifugalization, is determined. The experiments showed that there is no difference in the union of quinin with mammalian or avian erythrocytes. Nonrespiring, nonnucleated "dead" blood-corpuses behave the same as nucleated cells. No difference in the absorption of quinin salt or quinin base is demonstrable with a variation in the hydrogen-ion concentration of the external liquid within the indicated limits. Experiments with yeast cells showed that only the free quinin base penetrates these cells. Further researches were undertaken on the respiration of bird erythrocytes, a measurable process taking place within the cells. Respiration was measured by a method described by von Warburg. This consists in measuring the partial pressure of oxygen during respiration, with adsorption of the evolved carbon dioxid in a vessel containing potassium hydroxid, while the cell suspension is kept in oxygen equilibrium with the gas space by agitation. Each experiment demanded three respiration vessels one of which was used as a thermobarometer, one for measuring respiration without quinin, and one for measuring respiration under quinin addition. The total volume of the liquid in the respiration vessels was 12 c. c. The blood-corpuses were added first. The respiratory process took place to 30° C. in thermostats, and to obtain pressure and temperature equilibrium agitation for ten to fifteen minutes with open faucets was required. The closing of the faucet marked the beginning of the experiment, whereas the poisoning commenced correspondingly earlier by addition of quinin. The reaction of the experimental mixture was regulated by one-third molecular phosphate mixtures. The standard quinin solution was hundredth-normal solution of quinin hydrochlorid in physiologic sodium chlorid solution. The experiments show increasing quinin action with increasing hydrogen-ion concentration. Arrest of respiration must therefore be referred to the action of basic alkaloids. Initially the arresting action increases with duration of time, but gradually tends toward an equilibrium at which it remains constant. These phenomena are observed not only with avian corpuses but also with erythrocytes ruptured by alternate freezing and thawing. In a series of experiments in which there was an acid, so that the concentration of the quinin base was relatively low, it was found that respiration is first stimulated previous to its arrest. It may be shown that when arrest equilibrium has set in arrest of respiration increases proportionately to the increase of quinin concentration.

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**An Experimental Investigation of the Pharmacologic Action of Quinidin.**

*D. E. Jackson, Alfred Friedlander and J. V. Lawrence, J. Lab. & Clin. Med., 7:311, March, 1922.*

The action of quinidin on auricular fibrillation is of great therapeutic importance. However, the dosage has not yet been accurately determined, and, even when the patient is kept under observation by means of a string galvanometer or polygraph, unfortunate, even fatal, results have ensued. A more complete knowledge of the action of  
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the drug and the indications for its use are therefore necessary. It has been ascertained by animal experiments that quinidin will check auricular fibrillation in about 50% of cases; in the remaining 50% the fibrillation may be changed to a flutter, or may undergo no change, or an apparent acceleration may occur.

In experiments to test the effect of quinidin on the vagus endings, by means of subsequent electric stimulation, it was found that a prompt complete inhibition of the heart was produced by stimulation of the right vagus nerve. This lasted longer in the auricle than in the ventricle; 1 mg. atropin promptly relieved the inhibition of the auricle and resulted in a marked increase in the rate and amplitude of its beat. The right vagus was again stimulated, but no inhibition ensued, indicating that the vagus endings are not paralyzed by quinidin, but that the inhibitory action of the vagi on the heart is actually increased by the drug. This is of importance in the checking of auricular fibrillation or flutter.

When adrenalin is injected intravenously into normal animals, followed by 1 or 2 injections of quinidin, and adrenalin is again given, it is found that the animals are strikingly less sensitive than at first to the action of adrenalin. This action on the sympathetic system is best seen in the blood pressure. After large or repeated doses of quinidin, adrenalin may be found to be less effective in raising the blood pressure than it was before the administration of quinidin. Both the kidney and the spleen decrease in volume following quinidin, perhaps due to the general fall in blood pressure, which also causes asphyxia in the medullary vasomotor center. The volume of the leg has been found to increase, probably due to the action of the drug on the peripheral vessels and on the capillaries. Small doses also produce a rise in pulmonary pressure, large doses a fall, which may be due to dilatation of the pulmonary arterioles and capillaries.

Quinidin acts on the musculature of the peripheral vessels and perhaps on the skeletal muscles, in a manner similar to that of its action on the heart muscle. The decrease in the power of adrenalin to raise the general blood pressure may indicate an action on the sympathetic innervation or possibly on the capillaries. This is of importance in many cardiac diseases.

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(1c—221)

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**The Glucosids of Strophanthus. (Continued)**

*M. Tiffeneau, Bull. d. sc. pharmacol., 29:124, 184, Paris, March, April, 1922.*

The crystallized strophanthin of Kombé has not come into general use, probably owing to the difficulty of its preparation. The various methods of identification of Kombé's crystallized and amorphous strophanthins are here discussed, with a view to their differentiation from ouabain. (1) The form of crystals is observed only in crystallized strophanthin. Typical crystals are shown in microscopical plates. (2) The rotary power of crystallized strophanthin varies from +28.7° to +30° according as it is in a 1 or a 2% solution; of amorphous strophanthin, from +12° to 20°; of ouabain, 24° to 25°. The test is of great importance. (3) Color reactions: application of concentrated (Sec. 1—Page 1096)

$H_2 SO_4$  (Helbing's method) to either form of strophanthin or to ouabain immediately forms a vivid green, which turns later to a brownish red. This result can be obtained for the strophanthins with a solution of 90 or even 80%, but under these conditions, ouabain shows no coloration at all. Addition of potassium bichromate or phosphomolybdic acid to strophanthin Kombé gives a blue reaction with a greenish tinge. The sulphuric-tungstic reaction is green in strophanthin, colorless in ouabain; the sulphuric-vanadic reaction, intensely green in ouabain, colorless in strophanthin. A solution of phenol in concentrated HCl (Dragendorff, Unverhan) causes strophanthin to assume a violet color, later becoming green. The substitution of resorcin (Richaud) for phenol causes strophanthin to become rose-color, while ouabain remains colorless. Alkaline solution of picric acid gives, in the cold, an orange color with ouabain.

The toxicity of crystallized and amorphous strophanthin is studied upon various animals (tables shown). The latter is found to be less toxic, in a ratio of 1:2 subcutaneously, 1:1.5 intravenously. The dog, guinea-pig and rabbit were found much more sensitive to the poison than the white mouse and rat. This is attributable in part to the weaker sensibility of the heart in rodents, and in part to a more destructive property in their serum. Tiffeneau has made experiments on dogs, as the animals nearest to man in reaction to poisons. He found that the lethal dose of crystallized strophanthin of Kombé given intravenously was 0.10-0.11 mg. per kilogram of body weight; of various amorphous strophanthins it averaged 0.18 mg. Crystallized strophanthin was about 1.5 times as toxic as ouabain.

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**Rapidity of Resorption of Gases in the Abdominal Cavity.**

*Werner Teschendorf, Arch. f. exper. Path. u. Pharmakol., 92: 302, Leipzig, March 10, 1922.*

Exact measurements of the time required for the resorption of gases in body cavities are not available although this question is not only of practical importance in artificial pneumothorax and artificial pneumoperitoneum, but also of theoretical interest, inasmuch as a knowledge of the diffusion rate of individual gases is important for the explanation of the processes concerned in respiration. The experimental procedure was as follows: From a small gasometer 100 c.c. of different gases were insufflated into rabbits, the time required for the resorption of the gas being observed in the roentgenograph. The following resorption periods expressed in hours were obtained: nitrogen 80, Pentane vapor 26, hydrogen 25, methane 25, oxygen 24, carbon monoxid 17, ethane 8, nitrous oxid 2, carbon dioxid 1. The period for hydrogen sulphid was five minutes (within which time the animals succumbed to paralysis of respiration), for ethyl chlorid five minutes, and for ether two minutes. Following ether and ethyl chlorid the animals showed slight analgesia. Narcosis was effected with an injection of 1—0.5 c. c. ether into a rabbit's abdominal cavity, with which 200 and 100 c. c. gas were developed, respectively: Resorption took place in conformity to Exner's law (the diffusion equals the absorption coefficient divided by the square root of the density of the (Sec. 1—Page 1097)

gas). Exceptions were oxygen and carbon dioxid, which were absorbed more rapidly than demanded by the law, as they enter into chemical combination with hemoglobin.

(1c—223)

(1c—223)

**The Action of Gases on the Isolated Small Intestine of the Rabbit.**

*Werner Teschendorf, Arch. f. exper. Path. u. Pharmakol., 92: 324, Leipzig, March 10, 1922.*

The action of gases on the intestine may manifest itself in 2 ways: either mechanically by distention or chemically. In the latter case the gases are absorbed directly by the intestinal mucous membrane, or else their resorption takes place in the dissolved state from intestinal juice or intestinal content. They may also enter the blood and the cells of the intestinal wall by diffusion. But according to Kan Kato, the latter process is not an important one, as appears from the following considerations:

The researches on pulmonary respiration show that diffusion must be considered in addition to absorption in gaseous exchange in the body. But if diffusion be determined theoretically or experimentally, very small values are obtained for it in the exchange of most gases, with the principal exception of hydrogen. Furthermore, the path through the intestinal mucous membrane is much longer than through the respiratory pulmonary epithelium, so that diffusion encounters greater resistance in the intestinal mucous membrane. Moreover, the gases penetrating the body cells in this manner remain inactive unless they dissolve in the cells or enter into chemical combination. Hence, gases that have penetrated into deeper tissue layers by diffusion can unfold their action only by absorption. Therefore the absorption of gases is determined by the absorption coefficient valid for the body temperature and the direct proportional factor of intestinal pressure. If, however, chemical combining capacity exists between the gas and the body fluids, gaseous absorption is regulated essentially by the affinity of the fluid for the gas and is more or less independent of the prevailing pressure. Finally, in the resorption of a gas in the intestine, it cannot be a matter of indifference whether or not it is an atmospheric gas, inasmuch as the condition of absorption for a gas are the more favorable the lower its partial pressure in the blood. But even gases whose volume is sufficient to cause great intestinal inflation will generally possess volumes too slight to produce phenomena in the whole organism, even with complete resorption, as absorption in intestinal vessels is accompanied by elimination in the lung. A general effect will therefore be produced only with prolonged new development or new supply of a gas in the intestine.

The chemical efficacy of gases, as regards their capability of being resorbed, will be chiefly a local one confined to the intestine itself. A piece of the rabbit's intestine, 3 cm. in length, was inflated with various gases in accordance with Trendelenburg's method, in order to study their action on the intestinal longitudinal and involuntary musculature. The intestine was first inflated with indifferent air, producing dilatation of longitudinal and annular musculature, which induced

contraction of longitudinal muscles followed by intestinal relaxation and diminished pendular movement. In the case of strong intestinal musculature the original distention was absent so that contraction of the longitudinal musculature set in immediately. The phenomenon occurred with special frequency in intestines that had become stronger from several fillings. Slight filling usually increased pendular movement. Fatigue of the intestinal piece manifested itself by intermittent peristalsis. Nitrogen, oxygen and hydrogen behaved indifferently like air. Carbon dioxid was mostly stimulating but likewise indifferent in some experiments. Hydrogen sulphid had a paralyzing action on the tonus of involuntary and longitudinal musculature. When hydrogen sulphid was allowed to act one minute, recovery of the intestine no longer followed. Methane, ethane, carbon monoxid, nitrous oxid and pentane vapor were without specific action. Ethyl chlorid induced increased tonus and appearance of pendular movement and peristalsis.

(1c—224)

(1c—224)

**The Influence of Food and Spices on the Pulse and Heart.  
New Biologic Facts.**

*M. Heitler, Wien, klin. Wochenschr., 35:263, March 23, 1922.*

Heitler found in 1904 that the pulse was stimulated if sugar or salt were applied to the tongue and depressed if vinegar or quinin were applied. He then tested the influence of foods and spices on the pulse.

The application of some organic or inorganic substance to the tongue causes increased cardiac activity and larger pulse, other substances cause diminished cardiac activity and smaller pulse, while still others produce no effect at all. The effects are produced by application of minimal doses to the tongue, and the effect is due to the influence on taste. Stimulating substances may be changed to nonstimulating bodies as, for instance, the depressant effect of unripe pears or lentils and the stimulant effect of ripe peas or lentils. Heitler made a systematic examination of plants in the same way and found that warmth also affects the action of the foods. Substances which have no effect may become stimulating if warmed. This effect is transitory. The action of saccharin and other bodies, containing both stimulant and depressant components, depends on the component which is most powerful. These substances are less active when in solution. Water which is not warm and not too cold has no effect. It is stimulating if warm and prevents the depression of the stimulating substance. The pulse is depressed if acids are applied to the tongue and stimulated if applied to the mucosa of the cheeks and palate. Depression is the result if the entire mouth is painted. Spices, with the exception of garlic and onions, have a stimulating effect. All foods are more stimulating in the fresh state than when cooked. Chewing with an empty mouth, i. e. the motion of chewing alone, causes depression of the pulse. Chewing reduces the stimulant effect of certain stimulants and increases the depressant effect of depressants. The eating utensils are also of importance according as they are made of porcelain or glass. Silver, gold and nickel are stimulating while lead, ordinary copper and Chinese white copper are depressant. Wood has no effect.

If a depressant is eaten after a stimulant, the depressant effect of the second substance occurs only after the stimulant effect of the

first substance has worn off. The effect also depends on the duration of the reaction of both substances and especially on the time of application of the depressant substance. The pulse does not become larger if a stimulant is taken while the effect of a depressant endures, but stimulation occurs after the depression period is finished if the effect of the stimulation lasts longer than that of the depression.

The entrance of the substances into the stomach also causes changes in the pulse, which correspond to the changes when the substances are applied to the tongue or mouth cavity. The changes in the volume of the pulse are more marked. These are not caused by passage of the substances through the esophagus. The stimulus changes in the pulse caused in the esophagus are very slight; the effect occurs immediately after swallowing, lasting only 4-6 beats; the pulse then returns to its previous volume.

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**The Relative Toxicity of Germanium and Arsenic for the Albino Rat.**

*F. S. Hammett, J. H. Muller and J. E. Nowrey, Jr., J. Pharmacol. & Exper. Ther., 19: 337, May, 1922.*

A comparison of the relative toxicity of germanium dioxid and arsenic trioxid for the albino rat showed that the former can be administered subcutaneously in doses up to 180 mg. per kilo of body weight of the experimental animal with no apparent harmful effects. The latter usually produced a fatal result when similarly given to mature, nonpregnant female animals in the ratio of 8 mg. per kilo of body weight. Moreover, the injection of arsenic trioxid solutions is followed by marked necrosis and sloughing at the point of injection, which phenomena do not follow the injection of germanium dioxid solutions. It was evident that germanium did not possess the toxicity for the living organism exhibited by arsenic. It appeared from these results that the albino rat is mere resistant to poisoning by arsenic than is man. Correlated data indicate that this difference is due to the difference in the degree of the protein metabolism of the two species.

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**Changes with Advancing Age in the Resistance of the Albino Rat to Arsenic.**

*F. S. Hammett and J. E. Nowrey, Jr., J. Pharmacol. & Exper. Ther., 19: 331, May, 1922.*

In young animals 60 to 90 days of age the fatal dose was 11 mg. per kilo of body weight, only one of this series succumbing to the lesser amount of 10 mg. per kilo. In rats ranging from 120 to 150 days in age the fatal dose for the average animal was 9 mg. or over, only one of this series dying from the smaller amount of 8 mg. per kilo. In rats 210 to 240 days old, 8 mg. was the fatal dose, but one dying from the lesser dose of 7 mg. per kilo. All the deaths occurred within twenty-four hours of administration. Just as the difference in resistance of man and rat to arsenic can be attributed in large part to a

difference in the respective rates of protein metabolism, so probably the same factor enters into the differences in susceptibility observed in rats of different ages.

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(1c—227)

**The Toxicology of Hydrogen Arsenid.**

*Hermann Führner, Arch. f. exper. Path. u. Pharmakol., 92:288, Leipzig, March 10, 1922.*

White mice were placed in a narcotic flask in which hydrogen arsenid was formed from calcium arsenid. First the minimal toxic dose for a definite period of respiration was determined. The animal's death followed in 34 minutes with a concentration of 3.137 mg. AsH<sub>3</sub> per liter air; in 140 minutes with 0.189 mg., in 260 minutes with 0.10 mg. With a concentration of 0.15 mg. per liter air, and inspiration lasting thirty minutes, death took place in from one to two days. From the latter concentration the animals took up 0.01 to 0.012 mg. arsenic, estimated as As<sub>2</sub>O<sub>3</sub> per gm. mouse. The toxicity of AsH<sub>3</sub> and As<sub>2</sub>O<sub>3</sub> when injected subcutaneously, is fairly equal. From a hydrogen arsenid dilution of 1.7 mg. to 10 liters air, the mouse stores 100 times its volume in the course of one hour. In this process one quarter falls to the skin, one quarter to the blood and one quarter to the viscera, excluding liver, lungs and heart.

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(1c—228)

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**Lead Studies: I. The Estimation of Minute Amounts of Lead in Biologic Material.**

*Lawrence T. Fairhall, J. Indust. Hyg., 4:9, May, 1922.*

Methods for the quantitative determination of lead in biologic material are few, usually restricted in application and greatly complicated, for many organic substances mask partially if not completely the ordinary analytic reactions of lead. In the method described the lead is separated as the sulphid, and estimated as the chromate, the most insoluble salt of lead known and with the purity of which there are few interfering substances. The material is first ashed, then dissolved completely in dilute hydrochloric acid. This solution is neutralized (with sodium hydroxid, using methyl orange as indicator) very carefully or some loss of lead will occur. It is then slightly acidified with hydrochloric acid (avoiding excess because of the slight solubility of lead sulphid in the presence of calcium chlorid and hydrochloric acid) and the lead precipitated in cold solution as lead sulphid with hydrogen sulphid. The washed precipitate of lead sulphid is then dissolved in 2-5 c. c. concentrated nitric acid, the solution boiled to expel hydrogen sulphid and neutralized. The solution is acidified with acetic acid and the lead precipitated as lead chromate by an excess of potassium chromate and boiled. After filtering and immediate thorough washing the lead chromate is dissolved in dilute hydrochloric acid, an excess of potassium iodid added and the free iodin formed by interaction with the original solution, calcium phosphate is usually precipitated when chromic acid titrated with 0.005 normal sodium thiosulphate solution.

If attempt is made to precipitate the lead directly as chromate in  
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the solution is boiled, and a slight precipitate of ferric hydroxid, which often forms, will cause high results owing to its adsorption of potassium chromate. For constant results the progress of ashing is important—it must be carefully conducted at a temperature well below full red heat to avoid volatilization of the lead. It may be accelerated by extracting the residue, after carbonizing, with hydrochloric acid and hot water. The removal of inorganic salts complicates the manipulation somewhat but as they greatly hinder oxidation the gain in time more than offsets this. After the carbon is oxidized a residue insoluble in concentrated acid or even in alkali most often contains lead phosphate and is readily soluble in tartaric acid upon the addition of a few drops of hydrochloric acid. In the case of urine, 2 liters are evaporated to dryness with a small amount of nitric acid. With small amounts of blood, bile or other fluids containing organic matter, the carbon may be oxidized by heating with a mixture of sulphuric and nitric acids. In the method of analysis careful attention to details is important as the ratio of lead to other organic constituents of the ash is frequently 1:10,000. The accuracy of this method was tested with solutions containing weighed amounts of pure lead chlorid, and the average absolute error found to be 0.02 mg., corresponding to the titration error, since one drop of the sodium thiosulphate solution is equivalent to 0.02 mg. lead.

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**Phenobarbital (Luminal) Poisoning. Report of Case.**

*John Phillips, J. A. M. A., 78:1199, April 22, 1922.*

Within the last two or three years phenobarbital (luminal) has been used extensively as a hypnotic and sedative in various nervous conditions. Although various investigators have protested against its use as too dangerous, and have called attention to the occurrence of severe dermatitis with alarming symptoms following the administration of phenobarbital, but little attention has been paid to these warnings. Phillips reports a case in which severe dermatitis with fever, sore throat, serious gastro-intestinal symptoms and nephritis resulted from the use of this drug, indicating that phenobarbital should be administered with great care. Since there is little difference between the therapeutic and fatal dose, phenobarbital should not be prescribed in single doses of more than 1½ gr., and not more than 3 gr. should be taken in twenty-four hours. A patient under this treatment should be instructed, to stop the drug on the first appearance of a skin rash or of any untoward symptoms, and report to his physician at once. The urine of a patient under phenobarbital treatment should be examined once or twice a week. The drug should not be dispensed by druggists except on the prescription of a physician.

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(1c—230)

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**Report of a Case of Lysol-Poisoning.**

*O. B. Ormsby, Illinois M. J., 41:371, May, 1922.*

The patient, a vigorous young man of about 25, who had swallowed about 2 oz. of lysol, was found in a delirious condition. He was at  
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once given 1/10 gr. apomorphin, a therapeutic mistake. He rapidly passed into an unconscious state, and vomited only a small quantity of fluid. Another physician was called and asked to bring a stomach tube, he also brought 2 oz. alcohol. The stomach was washed out a number of times with a weak solution of bicarbonate of soda, and after getting most of the free lysol the alcohol was poured in, washed out in turn, ending with about a half pint of milk which was allowed to remain in the stomach. The patient was rational on the following day. Urine, jet black in color, was voided the following evening. The flow of mucus from his lungs was profuse, about a pint in six hours. Next morning patient had a temperature of 103° F. and the mucus was streaked with blood. No signs of cardiac failure were present and no stimulants were used, aside from alcohol in the stomach washing. The patient made an uninterrupted recovery.

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**The Poisonous Properties of Colloidal Silica. I. The Effects of the Parenteral Administration of Large Doses.**

*W. E. Gye and W. J. Purdy, Brit. J. Exper. Path., 3:75, London, April, 1922.*

A number of medical memoirs on silica have been published; for the most part they are of chemical and therapeutic interest but there has been no systematic and thorough study of the pathologic effects which follow the administration of colloidal silica. With the latter end in view the authors undertook a series of detailed experiments. The effects obtained by intraperitoneal injections varied with the degree of dispersion of the silica sol. Doses of 1-2 mg. of freshly prepared sol killed a mouse, and 30 mg. killed a guinea-pig weighing 250 gm. Sol allowed to become opalescent and whose mobility had diminished killed a mouse in doses of 5 mg. and a guinea-pig in doses of 50-60 mg. The gel did not kill in doses that can be practicably administered.

The results after the intravenous injections of silica sol varied with the method of administration, for example when the total dose was administered at once or in fractions at shorter or longer intervals. When a single lethal dose was administered in fractions at short intervals, e. g. every half hour, the animal remained quite well until the last two or three portions were injected. After the last fraction it succumbed. If the sol was given in large but sublethal doses (40-60 mg. for a rabbit) at daily intervals, the animal died after three or four days, and under these conditions death was due to profound degenerative changes of the liver, kidneys and other organs, together with hemorrhages in the intestinal mucosa, tracheal mucous membrane, heart and elsewhere. Very large doses of sol caused death immediately due to clotting of the blood. Silica sol injected intravenously in rabbits in daily doses of 30-72 mg. caused death in two to four days. At necropsy petechial hemorrhages and profound degeneration of the liver, kidney and spleen were found. It is believed that the key to the pathologic changes in the organs is found in the destructive action of silica sol on the endothelial lining of the blood capillaries. Other cells are doubtless affected directly by the poison, but from the microscopic findings it is clear that the primary effect is on the vascular endothelium.

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**The Poisonous Properties of Colloidal Silica. II. The Effects of Repeated Intravenous Injections on Rabbits; Fibrosis of the Liver.**

*W. E. Gye and W. J. Purdy, Brit. J. Exper. Path., 3:86, London, April, 1922.*

This paper describes the results obtained by injecting rabbits at daily or weekly intervals with doses of 0.25-30 mg.; the large doses were given at weekly intervals. Seventeen animals were used, but the results of the injections were confirmed by experiments on others which are not reported in this paper. An equal number of normal rabbits were used as controls. In 8 animals 5 mg.  $\text{SiO}_2$  was injected daily. This was followed by fibrosis of the liver, enlargement of the spleen, and changes in the kidney resembling interstitial nephritis. Two rabbits received 0.25 mg.  $\text{SiO}_2$  daily. Microscopic examination of the liver in one showed delicate strands of connective tissue stretching between portal tracts. The other organs were unaffected. In the second rabbit the liver showed a great thickening of the capsule. There was no tendency for the connective tissue to pass in between the liver cells towards the intralobular vein. The capsules of the spleen and kidney were thickened.

One rabbit received 5 mg. silica sol weekly. On microscopic examination it was found that the excess of fibrous tissue in the liver was almost confined to the capsule. The kidney showed a thickened capsule, an increase in interstitial tissue, and changes in some of the glomeruli. It would appear from this single result that, in order to cause an abundant formation of connective tissue with this dose, the injection of silica must be repeated daily. If seven days are allowed to elapse between the administration of the doses, the lesions produced by each dose heal practically completely before the next dose is given. Weekly doses of 30 mg. were injected into 3 rabbits. A very definite fibrosis of the liver and degeneration of kidney were produced within a few months. From this result it is concluded that the damage to cells caused by 30 mg. is too extensive to be healed completely in one week, and that a chronic pathologic condition is induced, fibrous tissue being formed in the constant attempts at repair.

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(1c—233)

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**The Toxicity of Skatol.**

*William Salant and Nathaniel Kleitman, J. Pharmacol. & Expt. Ther., 19: 307, May, 1922.*

Twenty mg. of skatol in 0.2 c. c. acetone given to a frog weighing 46 gm., or 43.4 mg. skatol in 0.43 c. c. acetone per 100 gm., caused symptoms of severe intoxication within a few minutes and the frog died four days later. A dose of 30 gm. of skatol in 0.3 c. c. acetone injected in a frog weighing 42 gm., or 70 mg. skatol in 0.7 c. c. acetone per 100 gm., was fatal within thirty minutes. A third frog weighing 46 gm. which received 40 mg. in 0.4 c. c. acetone, or 88 mg. skatol in 0.88 c. c. acetone per 100 gm., died in three hours. The effects of acetone alone given to frogs used as controls showed that doses of

0.48 c. c., 0.98 c. c., and 1.02 c. c. per 100 gm. of frog were followed by recovery. Though symptoms were observed in the controls, they were less severe, and presented a striking contrast to those observed in frogs which received skatol with smaller amounts of acetone in proportion to body weight. Doses of 20 to 30 mg. of skatol dissolved in 2 c. c. of 50% acetone were given rapidly intravenously to 2 cats. The results on the cats were not very satisfactory, as the solvent in the quantities given produced considerable depression of the circulation, greater when the skatol was injected. When the skatol was given intravenously to a dog, the results were more definite. Different amounts were injected, and were controlled by tests with acetone alone. In the first injection 60 mg. of skatol in 1.2 c. c. acetone were given very slowly at first, then more rapidly. Blood pressure fell from 150 to 100 mm. Hg, this low level persisting about forty-eight seconds. Respiration on the contrary was stimulated. The effect was not due to acetone, since the injection of 1 c. c. acetone produced only a slight transitory fall of blood pressure, although the injection was made twice as rapidly as in the case of skatol. Another injection of 50 mg. skatol in 1 c. c. pure acetone made twenty minutes later, and injected in twenty-three seconds, produced a fall of blood pressure of about 50%. Though complete recovery followed, it took nearly seven minutes before the blood pressure reached the same level as before the injection. Respiration was depressed for a brief period, and was followed by stimulation of short duration. Depression of the circulation was also shown when another injection was made of 80 mg. skatol dissolved in 0.8 c. c. acetone. Blood pressure fell from 186 to 110 mm. Hg, the speed of injection being much slower, almost half. The slow recovery of the blood pressure in this case showed that the depression produced by skatol is likely to persist. Respiration, as in the previous injection, was temporarily stimulated, but was preceded by a brief period of apnea. When the effects of the injection of skatol are compared with those of 1 c. c. of pure acetone, although the latter was made in ten seconds, as compared with twenty-three and forty-eight seconds when skatol was injected, blood pressure fell only 34 mm. Hg (from 144 to 110 mm.), and recovered promptly. Acetone became more effective after repeated administration.

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(1c—234)

**Studies in Carbon Monoxid Asphyxia. II. The Growth of Neuroblast in the Presence of Carbon Monoxid.**

*Howard W. Haggard, Am. J. Physiol., 60: 244, April 1, 1922.*

Physiologic evidence indicates that, aside from its displacement of oxygen from the blood, carbon monoxid is as innocuous as nitrogen. The nervous sequels of the poisoning follow as one of a train of profound physiologic alterations, due primarily to the anoxemia induced by the combination of carbon monoxid with hemoglobin and exclusion of oxygen. Haggard has attempted in this work to obtain some direct evidence upon this problem by observing the action of carbon monoxid upon cultures of chick neuroblasts growing in vitro. The nerve cells under these conditions maintain their gaseous exchange directly through the plasma, in which they are suspended, without the intervention of  
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hemoglobin. By thus dispensing with hemoglobin, the asphyxiant action of the carbon monoxid is avoided. The concentration of the gas in the medium about the cells is determined solely by the tension of gas in the atmosphere with which the plasma is in contact. For this reason it is possible to expose the neuroblasts to far greater amounts of carbon monoxid than would be possible in the body. It was found that carbon monoxid even in concentrations of 79% had no ill effect upon growing nerve cells, but illuminating gas was demonstrated as toxic for neuroblast cultures in concentration of even as little as 0.1%, indicating that illuminating gas contains other toxic substance or substances.

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#### 1d. BACTERIOLOGY AND PARASITOLOGY.

(1d—250)

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##### Increasing the Staining Power of Anilin Dyes by the Addition of Other Substances.

*Karl Post, Münch. med. Wochenschr., 69: 509, April 7, 1922.*

Experiments to determine the extent to which the staining power of anilin dyes may be increased not only by the addition of anilin oil and phenol but of the so-called auxochromous group, showed that methylene-blue could be strengthened by glycerin, fuchsin S by lactic acid, formic acid, oxalic acid, and acetic acid, eosin by glucose and glycocoll, and orange C by acetic acid. The chief aim of the experiments was to determine whether the staining power of the ordinary anilin stains could be increased by the addition of combinations of the aromatic series which contain the auxochromous group. It was found that methyl-violet is strengthened by phenol; safranin, fuchsin and Congo-red by paracresol; Bismarck brown, malachite green, pyronin G, neutral red, nigrosin and eosin by pyrocatechin; orange G by hydroquinon; nigrosin, eosin, orange G and Congo-red by pyrogallol; methylene-blue, orange G and Congo-red by phloroglucin; methylene-blue, gentian-violet, pyronin G and Congo-red by anilin; methylene-blue, methyl-violet, malachite green, fuchsin (magenta) and Congo-red by phenacetin; methylene-blue, methyl-violet, gentian-violet, Bismarck brown, fuchsin S, nigrosin, eosin and orange G by adrenalin; methylene-blue, methyl-violet, Bismarck brown, fuchsin S, nigrosin, eosin and orange G by benzoic acid; methylene-blue, fuchsin S, nigrosin, eosin and orange G by sulphuric acid; methylene-blue, methyl-violet and fuchsin (magenta) by saccharin; methylene-blue, malachite green, fuchsin S, nigrosin, eosin and orange G by salicylic acid; Bismarck brown, malachite green, fuchsin S, nigrosin, eosin and orange G by protocatechuic acid; methylene-blue, gentian-violet, Bismarck brown, pyronin G, fuchsin S, nigrosin, eosin and orange G by gallic acid; eosin, orange G and Congo-red by alpha-naphthol; nigrosin and Congo-red by beta-naphthol.

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(1d—251)

**On the Nature of Mitochondria. I. Observations on Mitochondria Staining Methods Applied to Bacteria. II. Reactions of Bacteria to Chemical Treatment.**

*Ivan E. Wallin, Am. J. Anat., 30:203, March 15, 1922.*

The materials used in this investigation included a large number of strains of bacteria, some from known pure cultures and others from various mixed infections, which included sputum from hospital patients, pus centrifuged from urine and pus from a carbuncle. The staining methods employed were Bensley's acid-fuchsin methyl-green, Schidle's modification of Altmann's, Benda's crystal-violet, the copper-hematoxylin, and the vital janus-green. In these staining methods, in which fixation preceded the staining, smears were made in the usual way on the slide. Before the smears had time to dry they were immersed in the fixatives of the different methods and later treated according to the procedure for the particular method. In a few instances bacteria were centrifuged, fixed en masse, embedded, and sectioned. The procedure in the janus-green vital staining followed the method used by Cowdry for blood-cells. The results show that the mitochondrial methods used are not specific for mitochondria, but that they also stain bacteria. The intensity of the stain was found to vary with the different strains of bacteria and with the different methods on the same strain of bacteria. Apparently such variations also occur with mitochondria. The janus-green vital staining method appeared to be the most delicate of those used.

In the second part of Wallin's study, a number of strains of bacteria were subjected to the action of alcohol, ether, chloroform, acetic acid, formaldehyd, potassium bichromate, osmic acid, and heat. The object of these experiments was not to determine the exact nature of the response of the organisms to these chemicals and heat, but to determine the effect on the staining reaction of the bacteria after such treatment. In every case controls were stained with the same stain used on the experimental preparations. The results show that bacteria may lose their staining properties when subjected to the action of certain chemicals ordinarily used in microscopic technic. The degree to which the staining reactions were affected varied with the different chemicals and also with the strain of bacteria. In many cases the bacteria retained their form, but were unstained, and in other experiments they were fragmented. In the cases where the organisms could not be seen, they apparently had been dissolved or fragmented. In the majority of experiments where the remains on the slide were granular and fragmented, these remains were stained. It is possible that mitochondria may behave in the same way and that some of the irregularly shaped mitochondria sometimes observed may be the fragments resulting from chemical action.

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**Comparative Studies on the Resistance of the Tubercl Bacillus and Kindred Bacteria to Chemical Decolorizing Agents.**

*H. Schlossberger, Gior. di clin. med., 3:121, Parma, March 20, 1922.*

This work is based upon the results obtained by Kolle and Schloss-  
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berger in experiments concerning the changes in the so-called acid-fast saprophytes after prolonged periods of growth in warm-blooded animals. By repeated passages through guinea-pigs the author succeeded in greatly increasing the virulence of numerous strains of acid-fast bacteria, nonpathogenic to the guinea-pig (hay bacillus, tubercle bacilli of cold-blooded animals), so that in time these bacteria caused a typical fatal generalized tuberculosis in guinea-pigs. This increase in virulence is associated with changes in staining properties (resistance to acid), and with biologic changes of the bacterial strains (the original strains, in the first days of incubation at room temperature, grow luxuriantly, but after a number of transplantations they exhibit the typical slow growth, at a temperature between 37° and 40°C., of the tubercle bacilli of warm-blooded animals).

The acid-fast properties of divers bacterial strains were studied, some of these before and after repeated passage through guinea-pigs, by the following technic: staining of slide preparations with warm carbolfuchsin, decolorizing with sulphuric acid in varying concentration (0.5%, 0.25%, 5%, 20%), or with alcohol (70% and 90%), or with aqueous solutions of sodium sulphite (0.25, 1, 20 and 26%), or boric acid (0.5, 1, and 5%); restaining with an aqueous solution of methylene blue or malachite green.

*Strains from Various Sources.*—The least acid-fast cultures are those of saprophytes. The so-called turtle tubercle bacilli (Friedmann's bacilli) show acid fastness equal to human or bovine bacilli; this is also true of avian tubercle bacilli. The degree of resistance of these various acid-fast strains to the decolorizing solutions bore no fixed relation to their origin; thus tubercle bacilli from the frog and snake were rapidly decolorized by sulphuric acid, whereas the Friedmann bacillus was as resistant as the human tubercle bacillus. On the other hand, Friedmann's bacillus was rapidly decolorized by sodium sulphite, whereas tubercle bacilli from frogs and snakes proved much more resistant, and the human bacillus was not decolorized at all. In like manner there were differences in behavior to these chemical substances between various strains of human tubercle bacilli and the so-called homogeneous strain of Arloing (the latter is only slightly resistant to sodium sulphite).

*Transplanted Strains.*—With the increase in the number of transplants there is an increase in the acid fastness of the strains, both of the saprophytes and of Friedmann's bacillus; the latter showed this markedly on exposure to solutions of sodium sulphite. Even strains of avian tubercle bacilli, after passage through guinea-pigs, exhibit increased acid fastness in the various concentrations of sulphuric acid, the different solutions of alcohol, and the solutions of sodium sulphite.

This demonstrates a close connection between virulence of bacteria and their resistance to acid. The author thinks that the increased virulence, the slow growth on culture media, and the other characteristics acquired by acid-fast strains of microorganisms after repeated passage through guinea-pigs, depend upon alterations in the physical structure of the bacterial cell, and that these alterations also manifest themselves in variations in the acid-fast properties of the bacteria.

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**The Vaselin Tube and Syringe Method of Micro Gas Analysis of Bacterial Cultures.**

*J. Howard Brown, J. Exper. Med., 35: 667, May 1, 1922.*

Reports by other workers of the production of carbon dioxid by certain streptococci and by *Bacterium typhosus* are confirmed. Data are presented to illustrate the accuracy and technical possibilities of the method.

In addition to economy of glassware, media, and labor, the vaselin tube and syringe method of micro gas analysis possesses the following advantages: (1) the gas produced above either liquid or solid media may be measured and analyzed; (2) the gas produced may be measured in terms of a definite and constant quantity of medium used; (3) the vaselin tube provides a closed system from which gases do not escape into the air; (4) separate determinations of the carbon dioxid produced in and above fluid media may be made; (5) determinations may be made from very small samples of material; (6) numerous gas analyses of the same culture may be made at various times during the growth of the culture without contaminating or destroying it; (7) gas production may be observed under both anaërobic and controlled aërobic conditions.

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**The Use of Phenol Red as an Indicator for Milk and Sugar Media.**

*H. C. Brown, Lancet, 202:842, London, April 29, 1922.*

Because of the difficulty experienced at times with litmus in demonstrating acid or alkali production in bacterial cultures, various formulas have been suggested to obtain a reliable litmus solution. McIntosh described a litmus which has proved to be the most satisfactory. As a substitute for litmus milk the preparations of phenol-red milk is made with condensed milk.

As an indicator for sugar media the same arguments hold good in regard to the use of phenol red instead of litmus. Small differences in reaction are more clearly shown on account of the increased sensitiveness of the former reagent. The author found in all of 5 strains examined that an initial acidity is produced when the sugar reaction of *B. dysenteriae* (Shiga-Kruse) is studied in a maltose-phenol-red peptone water. Although various methods of sterilization were tried, he still found initial acidity in all the strains. Duncan, of the London School of Tropical Medicine, though unsuccessful in detecting small changes in the reaction of cultures of different yeasts with litmus, found this indicator useful. The method is not intended to determine the terminal hydrogen-ion concentration, but owing to the vivid alterations in color and the ease of preparation, it may solve some of the difficulties met with in using litmus.

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**Activation by Lactic Acid.**

*Carl Timm, Ztschr. f. Immunitätsf. u. exper. Ther., 34:71, Jena, March 21, 1922.*

According to Much the addition of lactic acid to bouillon renders  
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hay bacilli grown in the latter virulent for mice. Injected intraperitoneally or subcutaneously the hay bacillus is noninjurious. Also, a suspension of hay bacilli injected together with 0.1% lactic acid solution into mice does not render the bacilli virulent as in the case of *Proteus* and *Mycoides*. But when hay bacilli were grown in 1%, 0.1% and 0.001% lactic acid bouillon, they become pathogenic for mice. The mice generally died after twenty-four hours and the autopsy showed a slight serous exudate in the abdominal cavity, but it was possible to obtain pure cultures of hay bacillus from the abdominal cavity as well as from the heart's blood. A mere acid action could not be involved here, as death supervened also when lactic acid bouillon with alkaline reaction was employed. No toxic substances had formed in the bouillon. In all cases death, taking place twenty-four hours after infection, was referable to the hay bacillus itself. This virulence is a transient property and disappears if the cultures from animal corpses are allowed to stand at room temperature. In the same way an agar culture derived from a lactic acid bouillon culture becomes harmless.

The new factor in these experiments is the observation that ordinarily harmless organisms are able to assume strong virulence under certain artificial conditions and that this virulence is dependent on chemical substances.

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#### Collodion Sacs for Aërobic and Anaërobic Bacterial Cultivation.

Frederick L. Gates, *J. Exper. Med.*, 35:635, May 1, 1922.

Ascitic fluid or dilute blood serum combined with fragments of fresh animal tissue forms a suitable medium for the isolation of highly parasitic organisms, but with the disadvantage that protein precipitates are formed from autolysis of the tissue fragment, which may obscure the view or stimulate or mask the presence of significant bodies, a disadvantage that is most noticeable in the search for minute undiscovered microbes or for filter-passing organisms such as the globoid bodies or poliomyelitis or *Bacterium pneumosintes*. To avoid this difficulty in the cultivation of the last named organism Gates found it practicable to place the tissue medium in a collodion sac surrounded by distilled water or salt solution, on the theory that the nutritive substances of the medium would diffuse through the sac wall and support growth in the surrounding fluid. Two designs of apparatus were developed, one to hold about 10 c.c. of medium for routine work, and the other to hold 50 c.c. for mass cultures. These can be used for either aërobic or anaërobic cultivation, and permit frequent examination of the cultures without disturbing the anaërobic state.

For the smaller amounts a V-shaped glass tube, similar to the Smith fermentation tube, but open at both ends, is used. The sac almost fills one limb of the V and is surrounded by the dialysate fluid. The mouth of the sac is shrunk on a glass tube sealed into the V tube with a rubber collar. For anaërobic cultivation the medium and the fluid are layered with vaselin. For molds in making the sacs short round-bottom test-tubes are used. These are lined first with a thin coat of 10% solution of gelatin, preserved with 0.3% cresol, and then with a thick collodion solution, the first layer being dried over an air

jet before the second is added. The method recommended is to slip the tubes to the lip through holes in a rubber stopper exactly fitting the mouths of three cylindrical jars, one containing the gelatin, one the collodion and one alcohol. After the molds and the stopper are fitted into one of the jars, it is then inverted for a moment so as to allow the solution to fill the tubes and then turned back so that the excess drains off. When the collodion has set the molds are filled with alcohol and rinsed with cold water. A glass tube is then fitted to the sac and the whole is put in warm water which shrinks the collodion on the tube and softens the gelatin so that the sac slips out of the mold. It is then inserted in the V tube. For mass cultures, the molds used are 50 c.c. Erlenmeyer flasks. Careful determination of permeability is important. A commercial collodion is employed, which has been evaporated in a partial vacuum until thick, and a sufficiently high degree of permeability is conferred on the membranes by immersion in 95% alcohol.

The Smith-Noguchi tissue medium is a more favorable medium for primary cultivation than the dialysate of such a medium obtained with collodion sacs. When growth in an artificial medium is established, however, it may readily be contained in the dialysate. The absence of precipitate makes it possible to collect for antigenic and serologic purposes a sediment composed of the microbic bodies alone.

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**A New Simple Indicator of Oxygen and Cultivation of An-aërobic Bacteria.**

*M. van Riemsdijk, Nederl. Tijdschr. v. Geneesk., 66:1423, Haarlem, April 8, 1922.*

Because oxygen acts as a poison for anaërobic bacteria, various measures have been used to remove oxygen from the atmosphere in which anaërobes are cultivated (pyrogallic acid in an alkaline medium, aspiration of air and replacement by hydrogen or nitrogen, etc.). The author favors the old method of Buchner (with pyrogallic acid), but a color indicator must be used to test for the total absorption of oxygen. Pyrogallic acid had an action upon methylene-blue but after two weeks the blue coloration had entirely disappeared when paper slips impregnated with methylene-blue were hung up in the atmosphere saturated with vapors of that acid. Upon opening the cylinder and admitting air (oxygen) the color returned with its pristine intensity.

Experiments show that methylene-blue was too tardy an indicator. Glucose in alkaline solution was 4.2 c.c. of a 10% solution of glucose; 0.1 c.c. normal NaOH, and 0.1 c.c. methylene-blue (50 mg. to 30 c.c. distilled water).

Double strips of hydrophile gauze are put in the glucose, alkaline and methylene-blue solution and after forty minutes all oxygen has disappeared from the pyrogallic-acid medium (at 37°C.).

To cultivate anaërobes, large glass receptacles were used; the oxygen is driven off from the culture medium by boiling it and then submitting it to a spout of cold water. Small pieces of liver tissue which, according to Tarozzi's experiments, absorb oxygen, are placed

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on the surface of the culture medium, and the tubes placed in the large pots containing the pyrogallic acid.

By this procedure and with the help of the methylene-blue indicator one can cultivate anaerobes away from the oxygen.

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**Differentiation and Identification of the Sporulating Anaerobes.**

*Ivan C. Hall, J. Infect. Dis., 30:445, May, 1922.*

Hall has made a taxonomic organization of the anaerobic bacteria based on a study of 73 pure strains, all but 4 belonging to 15 species. A new species, *B. centrosporogens* has been identified. Emphasis is laid on the importance of absolute purity as an underlying principle in the classification of anaerobes. Both surface-colony and deep-colony methods of isolation were practised successfully, but experience teaches the superiority of the latter for most cultures. Misnamed and anaerobically contaminated cultures are frequently received from various laboratories. The criteria necessary for identification in the order of their proper utilization, with respect to their significance, technic, and limitations, are: morphology, cultural reactions, action on proteins, action on carbohydrates, and pathogenicity. These points are utilized in the setting up of a differential key that can be used in the identification of the forms most commonly encountered, such as *B. bifementans*, 3 strains; *B. welchii*, 6 strains; *B. centrosporogenes* (new species), 4 strains; *B. butyricus*, 2 strains; *B. botulinus*, Type A, 2 strains; *B. botulinus*, Type B, 3 strains; *B. sporogenes*, 24 strains; *B. histolyticus*, 1 strain; *B. chauvoei*, 1 strain; *Vibrio septique*, 7 strains; *B. novyi*, 3 strains; *B. tetani*, 7 strains; *B. putrificus*, 3 strains; *B. tetanomorphus*, 1 strain; *B. sphenoides*, 1 strain; *B. tertius*, 1 strain.

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**Remarks on the Work of Bruno Lange: "The Significance of the Media Employed for 'After Culture' in Determining the Success of Disinfection."**

*K. Suepflé, Ztschr. f. Hyg. u. Infectionskr., 95:370, Berlin, March 20, 1922.*

In a study by Bruno Lange, to confirm the importance of after culture, in determining the success of disinfection, it was stated that in tests with anthrax spores the employment of optimal culture media was decisive, but in his experiments with staphylococci, a favorable influence followed the addition of glucose to the bouillon, even if evidence was nevertheless less marked than was to be expected from the work of Suepflé.

These discordant results are due to a somewhat different technic from that used by Lange who worked always with phenol, grotan and sagrotan and tricresol and with an extraordinarily small number of organisms. Nevertheless his experiments showed that the 3% glucose bouillon has a favorable effect in bringing about an increased growth in individual staphylococci. Whether it is correct in judging disinfection to take the washings in all cases so closely as in the experiments carried out by Suepflé will be discussed in future communications.

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**Conductivity of Bacterial Cells.**

*R. G. Green and W. P. Larson, J. Infect. Dis., 30: 550, May, 1922.*

In investigating the method of measuring the permeability of cell membranes by determination of the electric conductivity of cells, Green and Larson, working with *Bacillus coli* and *Staphylococcus albus*, found that dead bacterial cells offer a resistance to an electric current that is almost, if not entirely, equal in amount to that exhibited by live bacterial cells. Bacterial cells growing in ordinary mediums store up diffusible salts within their bodies to a greater concentration than is found in their habitat. When these cells are killed by heat or by formaldehyd an exchange of salts takes place between them and the surrounding medium. In these experiments the drop in resistance on cell death was shown to be due chiefly to an exosmosis of salts into the surrounding solution. On the death of bacteria there is, also, a definite decrease in the size of the cell, with the result that less space is taken up by these cells between the electrodes, and since the bacteria have a higher resistance than the surrounding solution there is a corresponding decrease in total resistance. From these findings it appears that conductivity measurements do not measure a change in permeability of bacterial membranes, but that permeability is indicated only by the exosmosis of salts from the cells killed by heat and by formaldehyd.

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**A Mutation of *Bacillus Anthracis*.**

*Alfredo C. Marchisotti, Semana médica, 29: 622, Buenos Aires, April 20, 1922.*

The so-called mutations of *Bacillus anthracis* previously described have generally been simple variations obtained by various artificial means, and not true mutations. The mutations observed by Marchisotti relate to the morphology of the organisms, and of the colonies, and to their cultural characteristics when grown on peptonized broth. They appeared suddenly in cultures one or two months old; when they were transplanted to solid media the special characteristics of the colony suggested contamination of the original culture. The newly acquired characteristics were fixed and transmissible by heredity. The new organism presented the morphologic and staining characteristics of *B. anthracis*, but the chains were much shorter, each of the links had blunt ends, and the distance between them was greater than in the normal strain. Sporulation was less marked. When cultivated in peptonized broth the organisms did not form balls, as is usual with cultures of this species. After eighteen hours at 37° C., small clusters appeared, which were difficult to dissociate. They did not cloud the liquid, and remained suspended at various levels. They resembled broth cultures of streptococci, except that the clusters were longer. When the clusters were broken up by agitation the medium was uniformly clouded, but cleared following decantation. The clusters gradually settled in the bottom of the tube, forming a powdery sediment. After several days at 37° C., the sediment became coherent; when agitated it rose in  
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spiral waves, remaining in contact with the bottom of the tube, as is observed in old cultures of staphylococci.

Growths on agar-agar differed greatly from the original strains, and were characterized by an abundant production of mucus. The strata were white, damp, glossy, without adhesions to the medium, and had sharp, regular borders. A ridge was noted in the central portion and along its entire length.

The virulence of the strain was variable, and depended upon the degree of attenuation of the original strain. When the organisms proved fatal to laboratory animals an edema was noted, of slight extent, which did not resemble the edema caused by inoculations of the normal strain. Immunization tests with the new strain proved variable and on the whole, unsatisfactory.

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**Bacteriologic Researches on Influenza.**

*B. Gosio, Ann. d'igiene, 32:1, Rome, Jan., 1922.*

Gosio has carried on extensive researches for three years on the pathogenic agent of influenza. He maintains that the Pfeiffer bacillus separated from associated types is of primary importance.

Association with flora favorable to its development explains its invasion, especially through the air, sometimes with very severe infectious results, which in microscopical findings may appear more largely due to the associated forms than to the Pfeiffer bacillus itself. On the other hand, the absence of associated flora explains the extremely curious cases of immunity in individuals greatly exposed to the contagion. The characteristic most peculiar to the biology of the influenza bacillus is its toxicogenic power, which is brought about either by the very high toxicity of the bacterial cells, or by typical leukocytic digestion, followed by absorption. The second phenomenon is the extreme leukotropism which characterizes the bacillus, by which the so-called cytological defense is broken down and the leukocytes actively take up the bacterial toxin.

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**The Biology of the Influenza Bacillus.**

*Kaethe Frankenthal, Biochem. Ztschr., 128:122, Berlin, March 7, 1922.*

Histidin may replace hemoglobin in the influenza bacillus culture. As a number of microorganisms are able to form histamin from histidin, influenza bacilli were examined for this. Histidin can be detected biologically by its reaction on the uterus, but a method had to be employed for the separation of histamin from peptone in the bouillon, for peptone also exercises a strong contracting action on the uterus. Nutritive bouillon (10 c.c.) was evaporated to dryness, the residue extracted with hot chloroform and hot absolute alcohol, filtered, the filtrate evaporated to dryness and the residue taken up in Ringer's solution. As this had no action on the excised guinea-pig uterus, no peptone was present. The experiments indicate that no considerable amounts of histamin are formed in the influenza culture. The utilization of histidin by the bacilli must therefore take place in another

way. Possibly the decarboxylation of histidin, which is apparently prepared for in this way, may be involved in those microbes to which histidin is unessential. In the case of influenza bacilli, on the contrary, it is possibly either assimilated directly, or first decomposed to the rings and then utilized.

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**Culture Media for Pfeiffer's Bacillus.**

*P. Calderola, Ann. d'igiene, 32:27, Rome, Jan., 1922.*

It has been satisfactorily demonstrated that a good medium for the culture of the influenza bacillus may be obtained with pigeon blood. The extreme preference on the part of the bacillus for the hemoglobin of the pigeon may be used as a criterion to differentiate true Pfeiffer from pseudo-Pfeiffer bacilli. The simplest method of preparing small amounts of pigeon-blood agar is the following. Several drops of 1% peptone water are drawn into a sterile syringe to prevent the coagulation of the blood; then, after previous preparation of the region, 2 c.c. blood is drawn from the axillary vein of the pigeon. This blood is diluted with 18 c.c. distilled water containing 1% peptone, and this is added to 3% agar in the proportion of 2:10. The preparation is heated at 60° C. for one hour. Pfeiffer's bacilli will grow in great numbers in this agar.

The brain is another excellent medium for the culture of this bacillus. A portion of the brain of some animal, of weight previously determined, is immersed in boiling water, where it is kept for ten minutes; it is then placed in a sterile porcelain mortar, reduced to a powder, and an equal weight of broth added. An emulsion of milky appearance is thus produced, which is passed through a metal net with meshes not too small to permit the passage of the small granules of the brain, and placed in a hot water-bath, where it is kept at 80° C. for half an hour; the emulsion is then combined with an equal amount of 3% neutral agar. The whole is sterilized with fractional sterilization at 60° C. In preparing the tubes and plates, it is necessary to mix the substances well, because the brain often settles to the bottom leaving only a stratum of agar at the top which does not permit the development of the bacteria. On the plates thus prepared there appear, twenty-four hours after fertilization, a number of very small, whitish colonies which double their diameter after thirty-six hours.

The liver, the spleen, and the kidneys also contain substances favoring the development of Pfeiffers bacilli. A rabbit is bled white and its liver, spleen, and kidneys removed. These organs are reduced to a very fine powder and diluted with physiologic solution in the proportion of 1:5.

The mixture is heated at 80° C. for half an hour. After it has been filtered through filter-paper, 1% glucose is added, and it is refiltered through Berkefeld's filter; the limpid fluid thus obtained is added to 3% agar in the proportion of 1 : 3. If the preparation is heated at a temperature greater than 80° C. the bacillus develops much less readily; this suggests that such temperature results in the destruction of some substance useful to the life of the bacillus or in the hydrolysis of those substances that favor its development. The affinity of Pfeiffer's bacillus for the blood of certain animals and not that of others, including man,

and the possibility of obtaining cultures with nonhematic media, would indicate that it is not the hematic pigment that favors the saprophytic life of this bacillus, but other substances which are found, for example, in the blood of the pigeon, as in the brain and in the parenchymal organs of all animals, in a physicochemical state such that it can be utilized by the microorganism.

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**The Differentiation of Pfeiffer's Bacillus from Similar Micro-organisms.**

*P. Caldarola, Ann. d'igiene, 32:32, Rome, Jan., 1922.*

On the basis of results obtained in the fermentation of carbohydrates and in agglutinations with diagnostic serums, Caldarola declares that, among the coccobacilli that have until now all been considered as Pfeiffer's bacilli, there can be distinguished one rather limited group of bacteria individualized by a combination of cultural and biologic properties. They are small bacilli, from 0.2 to 0.5 microns wide and from 2 to 3 times their width in length; they are immobile, never form spores, or become encapsulated; they may be colored slightly and are Gram negative. They never produce septicemia in animals; on the other hand, they are highly toxic to the guinea-pig and to the rabbit, in which they produce death by the action of their endotoxin. Animals whose brains are inoculated with these bacilli are attacked with acute encephalitis ending in death in from four to six days. They have great affinity for the blood of pigeons, and none, or very little, for that of other animals. They cause fermentation of levulose, glucose, and maltose, and never decompose arbutin.

Because of the immunity reactions which this group of bacteria produce with the serums of influenza patients, they should be considered the true Pfeiffer bacilli. It is possible to distinguish them from all morphologically similar bacteria by means of the criteria described above. Judged by these, it is not improbable that the so-called Pfeiffer's bacilli isolated in pertussis, from the pulmonary cavities of tuberculous subjects, in scarlatina, and in other diseases will be found to lack many of the properties of the true Pfeiffer bacilli, and the idea of the diffusion of Pfeiffer's bacilli in diseases other than influenza will be proved erroneous.

As with other bacteria, there are, besides, a number of varieties of Pfeiffer's bacilli, distinguishable by serologic criteria. The author has been able to recognize 2 of these varieties. This fact may explain the greater or minor seriousness of the infection, which varies not only with individual factors concerning the particular patient, but also with the degree of toxicity of the germ which provokes the infection.

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**Identification of Pfeiffer's Bacillus.**

*P. Zanelli, Ann. d'igiene, 32:38, Rome, Jan., 1922.*

Microscopical and bacteriologic examinations were made on 50 patients affected with influenza, for the purpose of identifying Pfeiffer's bacillus and of fixing the percentage of positive results. A positive  
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finding was obtained more frequently in examinations made immediately after the appearance of the first symptoms (during the first twenty-four to thirty-six hours) and upon the appearance of bronchopulmonary complications with mucous sputum mixed with blood. In 12 cases Pfeiffer's bacillus was found and isolation obtained in 10 by means of plate-cultures made with pigeon-blood agar.

*Microscopic characteristics.* In the mucous and purulent exudate, the Pfeiffer bacillus appeared as a tiny rod, from 0.2 to 0.3 microns wide, 2 or 3 times as long as wide, with slightly rounded or more often pointed, ends, immobile, and having no flagella and no capsule. Its pleomorphism is evident as regards dimensions. In artificial cultures on pigeon-blood agar, there were noted elongated, swollen forms, with slight central coloration, so that they resembled bacteria of hemorrhagic septicemia, with long filaments which still never assumed the spirillum-like form. It is not sporogenous.

*Staining.* It stains with difficulty with the common aniline dyes, well with a solution of phenic thionin, and rather better with Ziehl's solution, 1:5. A clear bipolar staining was never observed. It does not resist Gram's method.

*Cultural characteristics.* The bacillus is strictly aerobic, with most favorable temperature 37° C.; it does not grow in ordinary culture media. Experiments with blood agar show behavior varying with the kind of blood used: it develops well with the blood of rabbits, very poorly with that of guinea-pigs, moderately with that of the horse, very poorly or not at all with that of the ox or of the ram, poorly or moderately with that of the pig, and hardly ever with that of the dog. For human blood, Löwenthal's medium was used with extremely poor development. With medium of agar with the addition of frog's blood there was abundant development, with fish's blood none, with tortoise's blood none, and with snake's blood abundant development. Better results were obtained with media containing vitamins.

*Fermentative power.* Pfeiffer's bacillus slightly ferments glucose, maltose, and levulose; it does not modify a medium of arbutin.

The investigations were extended to normal subjects who presented no evident active morbid manifestations. There was never in any case any bacillus found in the primary respiratory passages, which resembled Pfeiffer's bacillus. On the other hand a bacillus similar to Pfeiffer's was isolated 6 times in 20 cases of catarrhal affections of the tonsils or of the pharynx, 5 times in 15 cases of acute bronchitis, and 7 times in 18 cases of chronic bronchitis. It was almost of the same dimensions, but approached rather the form of a coccus than of a bacillus; it did not resist Gram's method; but assumed the color with intensity, as it did also with diluted Ziehl's solution, 1:5. However, it presented the important differential characteristic of developing in common culture media; it fermented levulose and glucose and blackened the medium made with arbutin.

The same bacillus was isolated 30 times in 50 cases of pulmonary tuberculosis with positive finding for Koch's bacillus. In all these cases, the bacterium in question is probably a saprophytic one, partly and only morphologically similar to the true Pfeiffer bacillus, and one to which no pathogenic action can as yet be attributed.

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**Presence of *B. Lactimorbi* in the Throats of Cats.**

*Roger G. Perkins and James K. Shen, J. Infect. Dis., 30:505, May, 1922.*

The inference that cats are more or less frequent carriers of diphtheria has been drawn from reports of the occurrence of diphteria bacilli in the nose and throats of these animals. The authors, having already proved the possibility of confusion in cultures in human throats between *B. diphtheriae* and *B. lactimorbi*, attempted to extend their observations to cats to determine whether or not these reports were due to deceptive morphologic appearances. Two series were examined, 22 cats in all, swabs being made from the nose and throat, smeared on blood serum, and incubated for eighteen hours at 37° C. Stained preparations were examined for granules, and all apparently positive cultures were heated to kill the nonspore-forming organisms. *B. lactimorbi* was isolated in 7 instances. It appears, therefore, that there is a widespread distribution of *B. lactimorbi* under conditions that make it a frequent contamination accessible to the nose and throat, possibly in dust or in food. But since it is nontoxic its only importance from the standpoint of public health lies in the danger of false interpretation of the findings.

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**Behavior of Bruce's *Micrococcus* and of *Micrococcus Paramelitensis*.**

*E. Gerbasi, Pediatria, 30:289, Naples, April 1, 1922.*

In subjects clinically presenting the symptomatology of Mediterranean fever, it is sometimes impossible to demonstrate the specific agglutinins for the *Micrococcus melitensis*, while by blood culture a bacterium can be isolated that is morphologically identical with Bruce's micrococcus, but which differs from it in that it does not react to the specific serums obtained with *M. melitensis*. This bacterium is called *Micrococcus paramelitensis*.

Gerbasi has conducted researches to find out to what extent *M. paramelitensis* differs from ordinary *meliensis*. He took 4 types of *M. paramelitensis* isolated from patients with the clinical syndrome of Mediterranean fever and with negative serodiagnosis for *meliensis*. The investigations were morphologic, cultural, biologic, and serologic. He concludes that morphologically the 2 bacteria are identical; in the culture mediums, however, the *M. paramelitensis* develops more slowly and less abundantly. Biologic examination shows that the *paramelitensis* causes milk to curdle and sugar to ferment, while these qualities are not found in all types of the *meliensis*. The *paramelitensis* kept in a saprophytic state becomes capable of agglutinating with serums prepared with other types of the *meliensis*. It seems highly probable that *M. paramelitensis* cannot be considered as a separate class, but as a bacterium belonging to the family of the *M. melitensis* which, in the human organism, for some reason which we do not know, modifies its behavior in the sense that it does not provoke the formation of the agglutinins common to all the other forms of the *M. melitensis*, but only those specific for itself: it loses the property of becoming agglutinated by serums which agglutinate the other types, while it acquires that of curdling milk and

fermenting sugars with greater frequency and rapidity. Kept in a saprophytic state, however, it once more approaches the genuine *M. melitensis*, reassuming little by little its various characteristics.

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**The Relations between *Bacillus Melitensis* (Bruce) and *B. Abortus Infect. Bovum* (Bang).**

*J. Skaric, Ztschr. f. Hyg. u. Infectionskr., 95:358, Berlin, March 20, 1922.*

Great similarity has been demonstrated between the organism causing epidemic abortion in cattle and the organism of human Malta fever. These points of likeness concern the morphologic and cultural characteristics, as well as the immunologic reactions. The results were submitted to confirmatory study with 4 Malta strains and 8 cultures of the *Bacillus abortus*. Morphologically, these 2 bacilli showed no differences but far reaching similarities. They are apparently much more closely related to each other than typhoid and paratyphoid bacilli. The immunologic reactions showed differences but these were of a transient nature and did not exceed those variations found in various strains of bacteria. In saturation tests, acid agglutination and precipitation with a saturated aqueous solution of ammonium sulphate, they were alike. Complement deviation tests gave minimal differences.

What practical results are gleaned from these facts cannot yet be determined. Observations to date indicate that the *Bacillus abortus* is not pathogenic for man, though some American observers believe that the *bacillus abortus* in its passage through the body of the goat acquires a pathogenicity for man. But in the diagnosis of Malta fever, one must bear in mind that one may be deceived by a positive agglutination test, that the raw milk of abortus infected animals might have been partaken of and that the antibodies in evidence are formed against the *bacillus abortus*. It is established that not only can the *Bacillus abortus* itself be transmitted through the milk of infected animals, but also its complement-binding and agglutinating antibodies.

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**Studies of the Pneumococcus. I. Acid Death-Point of the Pneumococcus.**

*Frederick T. Lord and Robert N. Nye, J. Exper. Med., 35:685, May 1, 1922.*

Lord and Nye repeated some of their former work on the acid death-point of the pneumococcus, using a stronger broth in order to exclude the possibility of an unsuitable medium playing a part in the results reported. Their previous findings were, however, confirmed. At about pH 5.1 or lower the pneumococcus did not survive for more than a few hours: that about pH 6.8 to 7.4 it lived for at least many days, and at pH 6.8 to 5.1 it was usually killed with a rapidity which bore a definite relation to the hydrogen-ion concentration, i. e. the greater the acidity the more rapid the death.

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**Studies on the Pneumococcus. II. Dissolution of Pneumococci at Varying Hydrogen-Ion Concentrations. Effect of Temperature, Previous Killing of the Organisms, and Fresh Human Serum on the Phenomenon. Behavior of Other Organisms.**

*Frederick T. Lord and Robert N. Nye, J. Exper. Med., 35:689, May 1, 1922.*

In approximately isotonic standard solutions and in bouillon, suspensions of living pneumococci show dissolution of organisms in those solutions having higher than about pH 5.0. This dissolution is most marked at a critical range of about pH 5.0 to 7.0; some also takes place toward the alkaline end of the scale, although no dissolution occurs at the most acid end of the scale. In the standard solutions dissolution occurs at incubator, room, and ice-box temperatures, being less marked in the last. In standard H-ion concentration solutions dissolution takes place with pneumococci allowed to grow and die out in glucose bouillon, but unlike dissolution with living organisms it is progressive from the acid toward the alkaline end of the scale. Pneumococci killed by heat for one hour undergo less dissolution than living organisms, the general character of the curve being similar to that of living organisms. Pneumococci killed by heat at 100° C. for five minutes do not undergo dissolution. The addition of fesh human serum to suspensions of pneumococci at varying H-ion concentration prevents dissolution. Dissolution of pneumococci takes place more rapidly at pH 6.1 in standard solutions in which large numbers of pneumococci have been previously dissolved than in fresh standard solutions at the same H-ion concentration.

The dissolution of pneumococci under the conditions of the experiments may be ascribed, the authors believe, to an enzyme derived from the bacteria themselves. Other organisms, such as *Streptococcus viridans* and *hemolyticus* and *Staphylococcus aureus*, do not undergo dissolution under conditions similar to those to which the pneumococcus was exposed.

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**Studies on the Pneumococcus. III. Dissolution of Pneumococci in Pneumonic Cellular Material at Varying Hydrogen-Ion Concentrations. Resistance of Certain Other Organism to Dissolution.**

*Frederick T. Lord and Robert N. Nye, J. Exper. Med., 35:699, May 1, 1922.*

These studies show the effect of varying H-ion concentrations of cellular material obtained from the pneumonic lung on pneumococci and other organisms. Pneumococci of types I, II, and III undergo dissolution when mixed with cellular material from the pneumonic lung at pH 6.95 and 5.5 but not at pH 4.5. An enzyme derived from the bacteria themselves or from the cellular material may be the cause of the dissolution. *Streptococcus hemolyticus* and *Streptococcus viridans* do not undergo dissolution under similar experimental conditions.

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**Studies on the Pneumococcus. IV. Effect of Bile at Varying Hydrogen-Ion Concentrations on Dissolution of Pneumococci.**

*Frederick T. Lord and Robert N. Nye, J. Exper. Med., 35:703, May 1, 1922.*

The solubility of the pneumococcus in bile and in standard solutions may be due to the liberation of an enzyme from the bacterial cell. The process is more rapid in bile of a slightly alkaline reaction and in standard solutions of a slightly acid reaction, depending on a difference in the physical state of the bacterial cell under the influence of the 2 media. It is probable that bile can kill the pneumococcus with a minimum of injury to the cell membrane, thus enabling the endo-enzymes to operate at their optimum reaction, which is between pH 7.0 and 7.8. The fact that dissolution is more rapid in bile than in standard solutions is probably due to the more rapid death of the organisms in bile, with the liberation of a larger amount of enzyme at the optimum pH in bile than in standard solution.

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**Virulence and Mutation of the Bacillus of Rabbit Septicemia.**

*Paul H. De Kruif, J. Exper. Med., 35:621, May 1, 1922.*

The bacillus of rabbit septicemia appears in 2 forms, Type D, which is highly virulent, and Type G, which is of low virulence and rises as a mutant from Type D. The fixity of the virulence of the 2 types and the relation that mutation bears to this function is considered. The technic was the same as that in previously reported experiments consisting in the injection of varying amounts of rabbit serum broth cultures intrapleurally into young rabbits.

Type D possessed marked fixity of the character of virulence. This was observed both when cultures were regularly transplanted and when they were subjected to unfavorable conditions. Type G forms which rose in the same culture exhibited characteristic lack of invasibility. There was no noticeable variation in virulence among different individuals of a given culture of Type D. The virulence of Type G could be raised to a considerable titer by animal passage, but such organisms do not lose their characteristic of granular growth, which rather appears to intensify by animal passage. The acid agglutination zone of Type G strains which have been passed through animals shows a marked broadening. Type D owes its superior invasive power, at least in part, to its antiphagocytic activity, a property apparently not possessed by Type G.

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**Is Antiformin Necessary for the Concentration of Tuberculous Sputum?**

*Edith Rosenkranz, Münch. med. Wochenschr., 69:434, March 24, 1922.*

Lorenz described the preparation of a solution of sodium hypochlorite which was supposed to replace antiformin in making the tuberculous sputum homogeneous. The solution is made with 215 gm. cal-  
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cium chlorid, 286 gm. sodium carbonate and 2 liters water. Lorenz found that the sputum was made homogeneous more quickly with sodium hypochlorite, that the sediment was more easily thrown down and that it was easier to make the sputum adhere to the slide. He prefers this solution to the more expensive antiformin. Rosenkranz made solutions of sodium hyperchlorite from 6 different kinds of calcium chlorid. The chlorin content in the various solutions showed considerable differences—0.2, 0.23, 0.31, 0.36, 1.6 and 1.77% Cl. Examination of a solution of antiformin showed a Cl content of 0.45%.

The following result was obtained in 50 specimens of sputum concentrated by means of both solutions: There was no difference in the number of positive results but the sodium hypochlorite solutions caused a more rapid and complete homogeneous change in the sputum than antiformin and the cellular components were destroyed more rapidly and more thoroughly. There was no apparent difference in the throwing down of the solid parts or in the adherence to the slide. All 6 solutions were equally effective in spite of the difference in Cl content.

The experiments showed that the cheap and easily prepared sodium hypochlorite solution is a good substitute for antiformin.

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**The Cultural Characteristics and Virulence of Mammalian Tubercle Bacilli, and the Circumstances under Which They May Vary.**

*A. Stanley Griffith, J. State Med., 30:139, London, April, 1922.*

The 2 types of tubercle bacilli (human and bovine) found in mammalian tuberculosis are readily distinguished by their pathogenic effects on certain species of animals and by their manner of growth on artificial media. The media used for determining the cultural characteristics are bovine serum 5%, glycerin serum, agar, broth, and glycerinated potato. The human type which grows luxuriantly on all these media, is called eugonic. All strains of the human type display the same uniformity in their manner of growth. The bacilli of the bovine tubercle grow less readily, and are called dysgonic. It is not possible to get a similar kind of growth with all strains of the bovine type. These differences between the human and bovine strains are maintained after the most prolonged subculture, provided the cultures are grown on media which contain no glycerin.

Investigations have shown that the rabbit is the most suitable laboratory animal for differentiating standard bovine from the standard human tubercle bacillus. When the standard dose of 10 mg. bovine tubercle bacilli is injected subcutaneously into a rabbit, a progressive general tuberculosis results which is fatal usually within ten weeks. The subcutaneous inoculation of 10 mg. or more of human tubercle bacilli rarely causes the death of the rabbit within three months. Undoubtedly man is susceptible to both types. The bovine tubercle bacillus is less frequently associated with the severe and fatal forms of human tuberculosis, but this is because the bovine tubercle bacillus invades the body almost exclusively by way of the alimentary tract, whereas the human tubercle bacillus gains access mainly by the channel

of respiratory passages. Ingestion is much less certain and less severe in its effects than inhalation, nevertheless bovine tubercle bacilli are able to produce all the chief varieties of human tuberculosis, and in children often causes a severe and rapidly fatal general infection.

When dealing with a strain which appears to diverge from the standard in any particular, it is essential to study it carefully when inoculated into rabbits and guinea-pigs. A diagnosis should not be based on the result of a single test, either cultural or animal. The variants which are most likely to be confused with each other are the dysgenic human strains with standard virulence and attenuated dysgenic bovine strains. A large number of attenuated strains, both of the human and the bovine type have been obtained in greatest abundance in the human being, almost exclusively in the external forms of tuberculosis, particularly in lesions of the skin (lupus and scrofuloderma.) It is clearly shown from investigations made by the author that the tubercle bacilli lose virulence subsequent to entry into the skin tissues.

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**Growth of Tubercl Bacilli in Fluid Egg-Yolk Media.**

*Eduard Boccker, Ztschr. f. Hyg. u. Infektionskr., 95: 344, Berlin, March 20, 1922.*

Besredka has reported a medium which is especially favorable for tubercle bacilli. This represents a 5% solution of the yolks of hen's eggs, in distilled water, cleared by the use of alkali. The yolk emulsion should be cautiously mixed until the appearance of a light opalescence with 1% solution of soda. To avoid contamination the eggs should be washed before opening, with carbolic acid after Dorset's method; its pole should be flamed, and opened with sterile instruments. The growth took place always in the fluid; surface cultures were not attempted. Evidence of growth is shown by Ziehl-Neelsen preparations. The bacilli were found constantly in clumps and for a long time, in finely wound bands.

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**Staining of Tubercl Bacilli for Differentiation from Similar Organisms.**

*Willy Bender, Deutsch. med. Wchnschr., 48: 381, Berlin, March 24, 1922.*

The acid-alcohol-fast property is the basis of the Ziehl-Neelsen stain, and separates the tubercle bacilli, the bovine strains, and those from chickens and cold-blooded animals, from bacilli found in milk and animal feces. It is a fact of some importance that organisms similar to the tubercle bacilli are found in the human body and may lead to error. Bender was able to avoid this error in many cases by counter-staining with alcoholic picric acid, which stain is performed as follows: Carbol fuchsin and the usual decolorization with 3% HCl alcohol; stain for one minute with alcoholic picric acid (saturated watery solution of picric acid and alcohol, equal parts). The yellow stain with picric acid is poor in material concentrated by means of antiformin in urinary sediment, and in removed sputum from children. All these

should be stained with watery methylene-blue (1:20) after treatment with the picric acid. The alcholic picric acid method is recommended for differential diagnosis in putrid bronchitis, suspicious urogenital or intestinal tuberculosis, cysts, softened gland material and in removed sputum from small children.

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**Rabbits as Experimental Animals for the Human Type of Tubercle Bacillus.**

*R. Arima, Ztschr. f. Tuberk., 36: 114, Leipzig, April, 1922.*

A moderately virulent strain of the human type of tubercle bacillus (Toneyama No. 2), was injected to the amount of 20 mg. into the parenchyma of the testicles of 3 rabbits, and in amounts of 10, 5, 1 and 0.1 mg. into 5 others. Ten of the animals died during the following year and the rest were killed at the end of the year. Four of the animals, in addition to severe tuberculosis of the testicle, showed tuberculosis of the lungs, spleen, retroperitoneal, bronchial and sternal lymph glands; some of them had also tuberculosis of the spermatic cord and prostate and 1, tuberculosis of the kidney. These changes, however, did not show progression, but rather a regressive tendency. In 1 rabbit the infection remained purely local. Seven weeks after the vaccination all of the animals that remained alive, without reference to the amount of bacilli that had been injected, were given injections of old tuberculin, diluted 1:10, half receiving 0.1 and the other half 0.25 c.c. All of the animals had fever, most of them over 40°C.

Conclusions: (1) Injection of comparatively small amounts of the human type of tubercle bacilli causes tuberculosis, in some cases progressive, in others local and regressive, depending on the amount and virulence of the bacilli. (2). Inoculation of the human type of bacillus into the testicles of rabbits makes possible the following of the progress or retrogression of the affection with the naked eye. The reaction to tuberculin shows that there is certainly a relationship between tuberculosis of the testicle and general immunity. Useless experiments on guinea-pigs can be given up.

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**Cultivation of Bacterium Tularensis on Three Additional Media New to This Organism.**

*Edward Francis, Pub. Health Rep. (U.S.P.H.S.), 37: 987, April 28, 1922.*

Cultures of *Bacterium tularensis* of human and ground-squirrel origin which have been carried one year on artificial medium other than coagulated-egg yolk grow well on cystin agar composed of beef infusion agar containing 1% peptone and 1% agar adjusted to pH 7.6 to which is added when needed 0.02 cystin plain agar plus a piece of sterile rabbit spleen 3 mm. in diameter which has been rubbed over the surface of the slant and left just above the water of condensation, and Loeffler's blood serum coagulated at 70°C. The same cultures failed to show growth on plain agar and in fermentation tubes containing beef infusion broth. Cultures in the fifth generation on these special (Sec. 1—Page 1124)

mediums caused acute death with typical lesions of tularemia in guinea-pigs, from which bacterium tularensis was then cultured on the same medium; these later cultures caused acute death in guinea-pigs with typical lesions of tularemia. Old cultures of gonococcus and B. diphteriae also grow abundantly on cystin agar.

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**Demonstration of Typhoid Bacilli in Butter.**

*Fritz Ditthorn, Ztschr. f. Hyg. u. Infektionskr., 95: 409, Berlin, April 5, 1922.*

The important differences stated in regard to the duration of time during which the typhoid bacilli may be detected in butter seems to rest on uncertain methods. Ditthorn, however, by mixing 2 or 3 drops of a twenty-four hour bouillon culture of typhoid bacilli with 70-80 gm. butter in a fluid state at 37°C. and then allowing the mixture to harden, demonstrated the typhoid bacilli over a much longer period of time. In butter, the longest period was one hundred and fifteen days; in the margarin tests one hundred and twenty-six days. The fact that in butter the bacilli can be demonstrated most abundantly and for a longer period of time from the interior than from the surface of the material must be ascribed to the more marked action of acids on the surface. In 12 of the 24 tests however, the typhoid bacilli could not be demonstrated by direct smear. Distinctly more favorable was the result of the concentration, with bile (10-20 gm. butter or fluid margarin at 37°C. were shaken up with 60 gm. bile). With this concentration, even after about six months, the typhoid bacilli could still be demonstrated.

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**The Classification of *Bacillus Paratyphosus B.***

*J. Fürth, Wien. klin. Wchnschr., 35: 337, April 13, 1922.*

The paratyphoid B bacillus has heretofore been difficult to differentiate. Weil and Felix found that bacilli of the typhoid, paratyphoid and proteus groups have 2 types of receptors which can be definitely distinguished from one another by their resistance to thermic and chemical action, antibody formation and combining capacity. That group of receptors which Weil and Felix called stable receptors on account of their greater resistance, combines only the corresponding group of agglutinins; therefore when these bacilli flocculate, the flakes produced are fine. The second (labile) group of receptors combines only the second group of antibodies and brings about flocculation in large flakes. Experiments based on this theory were made by Fürth with several paratyphoid B bacilli, from the results of which he came to the following conclusions: (1) Among the paratyphoid B bacilli, as well as among the O-forms of the proteus group, there is a strain which has only the stable receptors and whose immune serum therefore causes only fine-flaked flocculation: this is Meiselbecke's meat poisoner. It is nonmotile. (2) The meat poisoning *Bacillus breslaviensis* which, under the name of *Bacillus Flügge-Kaensch*, has been regarded as a type of the ordinary paratyphoid B bacillus, is serologically no more

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nearly related to the ordinary paratyphoid B bacillus than Gärtners bacillus is to the paratyphoid B bacillus. The difference in the small-flaked and large-flaked agglutination alone shows the difference between them.

For the sake of completeness it should be mentioned that paratyphoid B (Weil) and Aertrick's meat poisoner have, unlike the above-mentioned atypical paratyphoid B strains, some stable receptors of the first order. The relation is shown in the possession of common labile receptors of the second order which cause these strains to agglutinate one another. With reference to complement formation, the opposite condition prevails; in this no elation can be demonstrated between paratyphoid B and Aertrick; they have no common stable receptors.

If a serologic test is made of the paratyphoid B group from this point of view, it clears up both the results of Castellani's experiments (not hitherto explained), and also complement fixation; in addition, it establishes the classification of this group of bacilli on a firmer foundation. Moreover, taking the double type of receptors into consideration causes a change in the interpretation of Fürth's previous experiments, in which he thought he had demonstrated a transformation of one species of bacillus into another.

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**An Epizoötic among Guinea-Pigs Due to a Paratyphoid B. Bacillus.**

*Katherine M. Howell and Oscar T. Schultz, J. Infect. Dis., 30: 516, May, 1922.*

The authors report the appearance among their guinea-pig stock of an infectious disease of the type to which the name pseudotuberculosis has been applied, characterized by the occurrence of multiple tubercle-like lesions of the spleen and liver. More than 500 animals died before the disease was controlled. At the height of the epizoötic many of the guinea-pigs died without typical lesions but with positive blood cultures. Females were much more highly susceptible to spontaneous infection than males, pregnant females especially susceptible and among the latter purulent metritis was not infrequent.

A Gram-negative motile bacillus was isolated from the lesions and from the heart blood of the infected animals, which had the cultural characteristics of the colon-typhoid intermediate group; fermented xylose, arabinose, and dulcitol readily, quickly formed alkali in milk, and darkened lead acetate agar within twenty-four hours. The organism appeared to be immunologically distinct from the representatives of the 4 fixed species of the group, *B. paratyphosus A*, *B. paratyphosus B*, *B. enteritidis*, and *B. suis*, which were used for comparative study. It was agglutinated in low dilutions (1: 160) of a serum against the Jordan strain of human paratyphoid B, and was closely related to although not absolutely identical with, 2 guinea-pig and 1 rabbit strain received from another source. On inoculation into guinea-pigs, rabbits, white mice, and white rats it was found to be virulent. Immunization of the stock with a killed polyclonal suspension of the organism was apparently the means of controlling the outbreak.

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**Mutability of Vibrios.**

*Camilla Platz, Ztschr. f. Hyg. u. Infectionskr., 95: 365, Berlin, March 20, 1922.*

In accordance with the studies of Wasielewski and Kuehn on protozoa, Kuhn found processes of different form, some of which resembled network, which he designated as *B* (bacteria); thread-like structures which he designated as *D* (dendritic) forms; *A* (ameboid forms); and finally a coccoid form which he designated as the *C* form. In the *A* and *C* forms he believed he had stages in the development of the bacteria in the compass of a single generation, or parasites of a special kind which lived in a kind of symbiosis with the bacteria. The observations of Kuhn may be traced to the fact that with the technic employed in preparation, the microscopic material is distinctly less damaged than by the usual staining and fixation methods. His statements confirm, in part, the observations of Ermengem, Kitasato, Hueppe, Gotschlich, and Baerthlein who described involution forms, degeneration forms and mutation forms. The appearance of threads, small granules, and swollen globular structures are best explained as the result of influences of bacterial metabolism.

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**The Difference between El Tor and Cholera Vibrios.**

*R. Kraus, Münch. med. Wchnschr., 69: 499, April 7, 1922.*

In a work published by the author in conjunction with Pribram, Prantschoff, Russ and Fukuhara on El Tor vibrios, special characteristics were demonstrated which, in spite of the identical biological reactions of these 6 El Tor vibrios and those of cholera vibrios, justified their classification as different species. Some bacteriologists hold different opinions, although the theory of the absolute specificity of the biologic reactions has undergone considerable modification.

As evidence of the differences in the 2 kinds of vibrios the authors note the following: El Tor vibrios (specific and nonspecific) as well as other vibrios produce acute toxins; cholera vibrios do not. By means of the toxins of specific El Tor vibrios an antitoxin can be produced which neutralizes the acute toxins of El Tor and other vibrios and the toxins of cholera vibrios. El Tor vibrios, like so many other vibrios, produce hemotoxins. The antihematoxin produced with hemotoxins of specific El Tor vibrios neutralizes not only the hemotoxins of these vibrios, but also the hemotoxins of other vibrios. Analogous phenomena were demonstrated for the hemotoxins of anaerobic bacteria by Schlossberger and for dysentery toxins by Pribram. Cholera vibrios do not produce hemotoxin. El Tor vibrios have a hemolytic action on blood plates (10% goat's blood), while cholera vibrios are hemodigestive.

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**A Brief Note on the Vibriothrix Zeylanica (Castellani, 1904).**

*Igino Iacono, J. Trop. Med. & Hyg., 25: 100, London, April 15, 1922.*

In addition to a strain of Shiga-Kruse bacillus, Iacono isolated from the stools of a patient with bacillary dysentery a peculiar pleo-  
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morphic germ with the characteristics of the organism described by Castellani as *Vibriothrix zeylanica*. This organism, as already noted by Taylor, Castellani, Anigstein, and others, is not pathogenic, but has a certain practical importance for the clinical bacteriologist, as on superficial examination it might be mistaken for a member of the true dysentery group as its colonies on colored special mediums, such as MacConkey, Drigalski-Conradi, Endo, are very similar to those of the dysentery bacilli. Gas or acid was not produced on any sugar broths. Microscopically, the organism showed the morphologic characters of a vibrio, a bacillus and a spirillum. The organism was not agglutinated by the blood of the patient from whom it was isolated, nor by the blood of other cases of dysentery.

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**A Research Study of Mumps.**

*Solomon F. Hoge, J. Arkansas M. Soc., 18: 190, March, 1922.*

In animals receiving injections of centrifuged sputum, blood or serum from mumps patients, the first definite increase of leukocytes and elevation of temperature appeared between the sixth and eighth day. The stadium of the curve was quite constant. The base line of normal for all the animals was reached by the twenty-ninth day. This gave an "incubation period" of about 7 days, a curve of from 17 to 20 days, a disease period lasting from 24 to 27 days. The control animals and those injected with the centrifuged sputum collected later than five days after the beginning of the parotid swelling did not show these alterations. The blood gave results entirely comparable to that of the sputum. The difference between positive and negative reactions cannot be explained on the basis of the injection of organisms or of a foreign substance composed of a variety of substances (as the sputum), as the negative findings followed injection with centrifuged sputum which differed from that yielding positive findings only in regard to the time that had elapsed from the inception of the mumps till the specimen was secured. The blood from the patients yielding positive sputum readings also gave positive reactions. The animals injected with sputum from normal patients did not yield a curve that could be confused with those recorded as positive. One guinea-pig received 2 c.c. of serum from an active mumps case and gave what was termed a positive curve. After three weeks 2 c.c. serum from an active mumps case failed to produce a positive curve in the same animal, whereas another animal receiving 2 c.c. serum from the same patient ran a positive curve. A third animal received 2 c.c. serum from an active case and had a prompt and vigorous reaction, evidently from the introduction of a foreign protein. The leukocytes increased to 23,000 by the third day, but on the twelfth day the count was below 13,000. From then on the leukocyte count and the temperature readings produced a curve in major points quite like the positive mumps curve. A month later this same animal was given 2 c.c. of serum from a patient who had had mumps some years before, but the second curve was negative. The control animals receiving pure cultures of the isolated organisms, recovered except one that died of streptococcic septicemia. The experiments tend to disprove a bacterial etiology.

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**Studies in the Cell Changes Specific for Variola and Vaccine.**

*H. A. Gins, Ztschr. f. Hyg. u. Infektionskr., 95:255, Berlin,  
March 20, 1922.*

Opinions vary in regard to the cell inclusions of Guanier, and the most diverse statements are to be found in the literature. By means of Paul's corneal inoculation, the possibility of more exact observations is afforded, and the point has been reached where the production of the Guanier bodies can be explained. The employment of Boeing's method of staining produces an appearance which seems to indicate that the Paschen bodies arise from the Guanier corpuscles. The observations on the Guanier bodies were made on the corneas of rabbits experimentally inoculated with variola or vaccine virus, on guinea-pig corneas after vaccine infection and on the skin of sheep after infection with true sheep-pox. The presence of the Guanier bodies was noted in 100 positive cases, while in 27 cases they were absent. Isolated Guanier bodies were found 19 times. In 29 cases there were the typical findings of numerous specific cell inclusions and in 25, wide sections of epithelium filled with large numbers of Guanier bodies. In 2 cases the change from variola virus to vaccine was followed by marked results. The pronounced aggressiveness of the variola virus toward the cornea of the rabbit seems to indicate that the change to vaccine will easily succeed.

As concerns technical proof of the Guanier bodies, special care is necessary. A good fixation is absolutely essential. To this end, the extirpated eyeball is placed in sublimate alcohol. After twenty-four hours, the cornea is separated; it is placed for one hour in 60% alcohol, then for twenty-four hours in iodin alcohol; on the following day, a half hour each in 70 and 90% alcohol, and one to two hours in absolute alcohol.

The method of staining is also important. Both the Giemsa and the Romanowsky methods are employed. For special purposes, the Mann stain, somewhat modified, may be used with good results. The Mann solution is made up as follows: 1% solution aqueous blue (Unna) 10 c.c.; 1% solution eosin (A. G.), 30 c.c.; distilled water 50 c.c. This solution is acidified with 5 drops acetic acid, allowed to stain for one hour, and then the specimen is differentiated in acid and alkaline alcohol. The Guanier bodies stain a red color and are beautifully differentiated from the nucleus, which is blue. It is important that the older Guanier bodies from foci of infection of from four to six days standing almost all show a reticular structure which is completely filled with very small granules. In distinction from the mature Guanier bodies, the young forms show few or no inclusions and the structure is for the most part homogeneous. Cell-inclusions which are specific for the vaccine and variola processes are found as soon as six to twelve hours after the infection. The epithelium is thicker, the basal cells are swollen; close to the nucleus of the epithelial cells there are frequently droplets which are stained blue with Biondi solution. Between epithelial cells which are well preserved and without inflammatory signs, but occasionally invaded by Guanier bodies, there are found peculiar structures which appear to have replaced epithelial cells. There are found

close knots of spherical or spindle-shaped corpuscles radiating from the center of the focus; and also in the immediate neighborhood of masses, stained dark blue, of broken up cell-bodies, or in the débris of such. The radiating structure and the centrifugal movement of the corpuscles is always striking, and on this account, the expression, radiating cell is used.

In these radiating cells further changes take place, the most important being that the corpuscles, freeing themselves from the center, make an effort to lodge themselves among the neighboring epithelial cells. Where this has taken place, one sees the corpuscles as free structures, elongated, between the cells, or where the pressure of cells is less, as round vesicles with unilaterally strengthened margins.

If the breaking up of the radiating cells advances further, one finds areas in almost every positive cornea which reveal numerous vesicles lying extracellularly, each of which attains almost the size of a red blood-cell, and has as a limiting membrane a thin wall which on one side in most cases is somewhat reinforced. This structure may be regarded morphologically as corresponding to the intracellular Guanier body and as regards staining reaction is not to be distinguished from it. That they have arisen from the radiating cells, one sees in those areas which show all transitions from the spherical body through the spindle-shaped structure to the mature forms. On the basis of this finding it seems firmly established that these vacuole groups are specific structures formed in the variola process in the rabbit cornea, and are identical with the cell inclusions known as Guanier bodies, from which they are to be distinguished only by the fact that they have not yet invaded, or been taken up by the cells.

The Guanier bodies reach the acme of their development seventy-two hours after inoculation. At this stage the epithelium is still half intact, and seeded with Guanier bodies. After four days nothing more is seen of the Guanier bodies. It is concluded that the Guanier bodies are not essential parts either of the cell nucleus or of the protoplasm, but must be regarded as independent, foreign bodies, which are encountered not only within the cells but also in case of recent infection between the cells of the epithelial layer of the cornea of the rabbit.

It seems likely that the Guanier body represents a characteristic form in the evolution of the variola and vaccine virus, and grounds for the parasitic nature of these inclusions are greatly strengthened.

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Animal Experiments with Spirochaeta Recurrentis.

G. Henning, *Arch. f. Psychiat. u. Nervenkr.*, 65: 225, Berlin, Feb. 9, 1922.

Experiments were made on mice and rats, by inoculation with the Hamburg race of the African Spirochaeta recurrentis (*S. duttoni*), in order to study the successive stages in the development of the spirochetes. The white mice were used for the breeding of a passage race of spirochetes some blood from the tail of the diseased animal being mixed with physiologic sodium chlorid solution and then injected intraperitoneally into other animals. The author first investigated the successive phases in the degeneration of the spirochetes. No compreh-

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hensive investigations had been undertaken on the behavior of the spirochetes in the different organs and at different stages of the disease.

In the spleen and liver, two separate lines may be distinguished simultaneously in the degeneration of the spirochetes, resulting (1) in involution forms and (2) in forms with a straight axis. The latter are found throughout the body of the animals in the veins and capillaries; but the involution forms are observed almost exclusively in the minute vessels of the liver and the spleen. It is only in these organs that the two forms are found side by side. The behavior of these forms was studied from the first attack of the disease through the crisis, the remission and the relapse. Although there is no strict correspondence between certain forms of spirocheets and certain stages of the disease, regular relations can be established. In the central nervous system, the spirochetes appear first in the pial veins, and soon afterwards in the small vessels of the nervous substance. During the height of the disease, several organisms are discovered in almost every field under the microscope, but few in number as compared with the liver and the spleen. During the intervals only a few elements, usually of smaller size and modified form, are found. During the relapses, they again increase but not to the number present during the first attack. An active migration of the spirochetes from the vessels was not observed. Spirochaeta recurrentis is not a tissue parasite. The behavior of the spirochetes was observed during salvarsan treatment through the various stages up to their disappearance from the blood.

The histologic changes in the central nervous system are not pronounced, which seems natural considering that it is only slightly involved in the invasion of spirochetes, and that the disease is of short duration. After the subsidence of the first attack of the disease, lipoid products of decomposition are found in the cells of the choroid plexus and in the ependymal cells of the lateral ventricles. They are also found in the endothelial cells of the pial and cerebral vessels. In later stages of the disease, these lipoids are sometimes also present in the ganglion cells, but as a rule only after several relapses. These observations serve to corroborate that *S. recurrentis* is not a tissue spirochete and is not neurotropic.

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**The Association of the Virus of Typhus Fever with the Various Blood Elements.**

*J. Ségal, Brit. J. Exper. Path., 3: 95, London, April, 1922.*

Experiments were made to obtain the virus of typhus fever in as pure and concentrated form as possible. Nicolle concluded from the results of earlier experiments that the virus of typhus fever in the circulation is contained within the leukocytes, the virulence of the plasma being due to the debris of leukocytes that it might contain. Ségal attempted to confirm this by producing a considerable extravasation of leukocytes by injections of sterile broth into the peritoneum of typhus infected guinea-pigs. In most cases the cells present in the exudate consisted entirely of leukocytes. Guinea-pigs were inoculated intraperitoneally with 4-5 c.c. of this exudate or with leukocytes obtained by centrifugalization of a similar volume of fluid and emulsified in saline solution. Negative results were obtained in all these experiments,

whereas infection ensued in the animals inoculated with a blood-containing exudate and in those receiving a blood or brain inoculum of the experimental animals.

As Kusama had demonstrated an intimate connection between the virus of typhus and the blood-platelets, the author carried out similar experiments on guinea-pigs. The procedure was as follows: The blood was received into a 2% citrate solution in saline solution containing 1% glucose, centrifuged five to seven minutes at about 3000 revolutions per minute and then allowed to stand overnight in a cold room. The supernatant plasma, having a milky appearance, was then carefully removed and centrifuged for forty-five minutes at about 6000 revolutions per minute. Microscopic examination showed this supernatant fluid to be cell-free and the white sediment consisted entirely of blood-platelets. Plasma carefully freed from cells proved noninfective even in large doses, whereas the inoculation of platelets invariably produced infection even with so small a quantity as that obtained from 1.5 c.c. blood. The separation of platelets from a large quantity of blood by centrifugalization will yield a high concentration of virus for experimental purposes.

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**Experimental Study of Typhus Fever.**

*Helena Sparrow, Polska gaz. lek., 1:239, Warsaw, March 26, 1922.*

In September, 1920, at the Epidemiological Institute of Warsaw 2 monkeys were inoculated with a brain emulsion from guinea-pigs which had typhus fever. They were kept under observation for four weeks and did not show any clinical symptoms or any marked change in general condition. After eight weeks, these same monkeys were injected with 3 and 5 c.c. defibrinated blood taken from typhus fever patients at the height of the exanthem. Even then there were no typhus fever symptoms and no change in the index of the Weil-Felix reaction. This surprising result indicates that the strain of typhus fever used, though still toxic for guinea-pigs had lost its toxicity for monkeys, but that it was still active enough to prevent an infection of these monkeys with human virus.

The author therefore resolved to test the infectiousness of this laboratory virus on herself. She gave herself an injection of 0.3 c.c. brain substance of a guinea-pig which was killed five days after having been inoculated with a virus that had been passed through 22 animals; twenty hours after the injection of the brain emulsion she gave herself a subcutaneous injection of 10 c.c. of an inactivated typhus fever convalescent serum. Ten days later she had headache and pain in the limbs, sleeplessness, increased excitability and slight rise of temperature. On the third day afterward, her temperature was 38.3°C., pulse 90. On the fifth day an exanthem of very small spots appeared on the thorax, back, abdomen, and very slightly on the extremities. A day later a pronounced eruption was present on the flexor surface of the extremities. On the eighth to eleventh days temperature rose to 39°, with a fall by lysis in three days. The pulse was 90 per minute; at the height of the disease it rose for a little while to 100. The Weil-Felix reaction was negative on the fourth day; on the ninth day it was positive with a dilution of 1:6400. There was clinical typhus fever.

The experiments showed that the disease produced in guinea-pigs by inoculation with blood from typhus fever patients is really typhus fever; that the virus can be transmitted for an unlimited time to animals that are susceptible to typhus fever, and that the strain, after 22 passages through guinea-pigs, keeps its virulence.

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Studies on Typhus in South America. Biologic Reactions.

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*R. Kraus and J. M. de la Barrera, Ztschr. f. Immunitätsf. u. exper. Ther., 34:1, Jena, March 21, 1922.*

Researches were undertaken to determine whether South American typhus differs biologically from European typhus. For this purpose the heat, serum, and tissue reaction were employed. The guinea-pig was chosen as the experimental animal as it is extremely sensitive to the typhus virus. As the fever temperature curve is to be regarded as the only clinical objective sign of the infection with typhus, it is essential to obtain an accurate knowledge of the normal temperature and its fluctuations in this animal species. The guinea-pig's rectal temperature in Buenos Aires is 39-39.5°C. whereas in Vienna it is 38°. Injections of blood of healthy human beings and of those suffering from chicken-pox and influenza do not especially affect the temperature of normal guinea-pigs, and no increase of temperature followed peritoneal injection of organic emulsions from healthy guinea-pigs. Following injection of typhus patients' blood 270 out of 416 guinea-pigs reacted with fever. 146 animals were refractory (35%). The incubation period amounted to seven days. This proves that typhus virus transmitted to guinea-pigs in South America (Peru, Bolivia, Argentine, Chili) induces a typical fever reaction, the same as in Mexico, Europe and Africa. Experiments showed that healthy guinea-pigs may be infected by contact with infected ones. In testing South American typhus with the Weil-Felix reaction it was shown that the former is to be ranked with the European, not only clinically, but also in regard to biologic reactions such as the heat and serum reactions. The Weil-Felix reaction is specific (dilution 1:100) and almost constant. Several cases are also communicated of reactivation of histogenic agglutinins which had remained in a latent state from an earlier infection and were reactivated by the new heterologous process. For instance, in a case of typhus, a typhus-agglutination of 1:10,000 was found, the patient having suffered from typhus about ten years previously. This was confirmed in the course of the attempts to obtain agglutinins in rabbits from Proteus X19 with the brain of infected guinea-pigs. But it is at any rate certain that the virus is as little able to produce anti-infectious antibodies against Proteus X19 in the guinea-pig, as is Proteus X19 against the virus. Weil-Felix's statements therefore demand further examination. Adsorption experiments with the agglutinating rabbit's serum obtained with infected brain, B. Proteus X19 and patients' serum, recall facts known to the science of immunity, namely that incongruity may exist between antigenic and fixative property. In precipitation, the serums behave toward the X19 filtrates as in the agglutination of X19. Regarding histologic changes in typhus, it was possible to show that perivascular infiltrates

in the skin and brain are present in infectious diseases that are etiologically entirely dissimilar, and therefore cannot be looked upon as specific for typhus. Such perivascular infiltrates occur in cerebrospinal meningitis, influenza, Borna's disease, protozoal diseases, sleeping sickness, mal de Caderas of the brain, hydrophobia, poliomyelitis, typhus, lethargic encephalitis, Volhynia fever, kedani disease and Rocky Mountain spotted fever.

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**Details of the Technic Adopted in Following Weigl's Plan of Feeding Lice Infected with the Virus of Typhus Fever by Rectal Injection.**

*A. W. Bacot, Brit. J. Exper. Path., 3:72, London, April, 1922.*

Bacot elaborates on the method of Weigl in feeding lice by inserting a minute capillary pipet into the rectal opening of the insect and injecting a meal of blood. Bacterial contamination of the gut is one of the normal causes of death when breeding lice in gauze-covered boxes. The dangers of infection can be minimized by sterilizing the lice before inserting the pipet. This is accomplished by immersing the insects from two to four minutes in 2% lysol at 60° -65°F. The lice are then transferred to sterile water and thence to filter paper placed in a Petri dish to recover. To perform the injection, the louse is held in position under a slip of paper on a glass slide placed on the stage of a microscope with the anal extremity projecting slightly. A fine capillary pipet is redrawn in a minute flame and the tapering end cut off at a point that will give an external diameter of about 0.1 mm. This capillary point is rounded carefully in the flame. After loading, the pipet is inserted in the rectal passage slightly beyond the last segmental incision and the fluid forced into the stomach by gradual pressure on a well-fitted rubber teat. As there is considerable danger of pricking the fingers they should be covered by a thin metal guard when working with infecting material. Before inserting the pipet the hairs surrounding the anus should be touched with a drop of 85% alcohol.

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**A New Causative Organism of Typhus?**

*Augustin Belai, Wien. klin. Wchnschr., 35:368, April 20, 1922.*

At the close of the year 1919 a few copies of a pamphlet were distributed in Siberia, written by the Russian physician D. I. M. Schestopal in which a causative organism of typhus discovered by him was described.

For examination one requires a little blood taken from a distinct cutaneous rose spot petechia. The skin is cleansed and scarified until blood appears, when it is again cleansed with ether and the blood drawn with Bier's bulb. With a sterilized oese the drop of blood is then placed upon an object glass and covered with a cover glass, the edges of which have been smeared with vaseline. A second preparation is taken from the same place after it has again been cleansed with ether; also a third. In the latter, examination is more difficult as it contains mostly serum and the spirochetes of the exanthema are found either in,

or combined with, erythrocytes, in contrast to the Spirochaeta pallida. To avoid coagulation quick work is necessary. One must take blood from different parts of the body, preferably from rose spots two or three days old. Dark field examination is essential as under a very strong light the spirochetes are not visible in one part of the mirror. The erythrocytes appear upon a black-yellow background in golden yellow heaps.

From these several or many motile pale blue spirochetes emerge. If found in one layer, attention must be directed to their motility so as not to mistake them for fibrin threads. After ten hours many spirochetes have lost motility; they resemble thin candles with a flame at the end (centrosoma). Under a suitable light one can recognize a capsule and spiral curve. Almost every spirochete is united with an erythrocyte as though it drew the latter toward it. As many as 6 spirochetes may emerge from 1 erythrocyte. The length varies from  $\frac{1}{2}$  to 5 diameters of an erythrocyte. The spirochete is thinner than the erythrocyte and contains more and smaller curves with a swelling at the end (Babes-Ernst bodies?). It is only in the affected areas of the exanthema, particularly in the second drop of blood, where the spirochetes are found united with the erythrocytes, therefore it is no accidental contamination.

The fact that the typical clinical picture can develop in recurrent exanthematous cases after the second attack of fever resulting from debility, is proof of the stability of the organism. It becomes apparent that this spirochete is at first retarded by the toxin created by Obermayer's spirochete and the high fever. Recovery is probably due to the formation of antibodies, the number of which may correspond to the high number of the infective agents, which also explains the subsequent lifelong immunity.

Dr. Schestopal names the spirochete in memory of his wife who succumbed to the exanthema: Spirochaeta Emiliae Schestopal.

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#### Experimental Research on the Toxic Action of Sporotrichum Beurmanni.

*Giuseppe Berti, Riv. di biol., 4:44, Rome, Jan.-Feb., 1922.*

Experiments were made with Sporotrichum beurmanni: (1) by subcutaneous injections of broth cultures of living Sporotrichum, with a view to studying the macroscopic and microscopic appearance of the sporotrichotic nodule; (2) by subcutaneous injections of broth cultures of Sporotrichum after passage through a Berkefeld filter, in order to determine the tissue changes wrought by the exogenous soluble toxins; (3) by subcutaneous injections of dead broth cultures of Sporotrichum after heating for an hour at 80°C. in the thermostat, in order to study the changes produced by all the toxins of the microorganism.

The first group of experiments confirmed the findings of other observers, i. e. the formation of a granuloma characterized by a central necrotic area, with numerous polymorphonuclear leukocytes in a rather good state of preservation, degenerated epithelial cells, and a small number of parasites; an intermediate zone consisting of migrating hypertrophic histogenetic cells, with an occasional giant cell; and an outer zone consisting of connective tissue of fibroblastic type.

Experiments of the second group showed that the injected fluid is rapidly absorbed and causes a nodule which disappears quickly (in 17 or 18 days). The neighboring lymph-glands apparently undergo no change, and aside from slight small-cell infiltration histologic examination reveals nothing striking. Exogenous toxins are present in minute quantities and are not very active. Their action is predominantly congestive, occasioning a transitory exudate of fluid and cells.

Experiments under the third heading yielded rather striking and constant tissue reactions about the points of injection, and resorption of the material injected was slow but complete, and one month later not a single nodule was found at the point of inoculation. The sclerosis following injection of all the toxins is more pronounced than that obtained under the first heading; in fact the predominating result after injection of the total toxins is a constant fibrous and connective tissue sclerosis.

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Rapid Staining of Intestinal Flagellates.

*R. Oehler, Deutsch. med. Wchnschr., 48:456, Berlin, April 17, 1922*

Ruppert's method of staining was a failure for spirochetes. For flagellates, the procedure is plainer. The intestinal contents are stirred into agar jelly at body temperature (1: 500 water), 2 or 3 loopfuls of this suspension are placed on a slide, where it is well mixed, spread out thinly like a blood smear, and left to dry. Two grams of brilliant blue 8 G. extra are dissolved in 100 gm. water. The stain is poured on the slide and slightly warmed; it is washed in water for a minute, dried, and enclosed in liquid paraffin with no after-staining. Bresslau's stain is a cover stain. A thick mass of Grüber's opal blue is mixed with the intestinal contents or pus and a thin smear made. It is dried by waving in the air. All elevated parts are pale and all depressions blue. There are various shades in relief on a dark blue background. Vital staining with Riegel's chloroform-azure is thus performed: Manson's solution medicinal methylene-blue Höchst 2.0 gm. with borax 5.0 gm. and water 100 gm. is shaken up with an equal amount of chloroform; the deepest blue chloroform azure solution is separated from the water methylene-blue by filtration and decantation. One drop of this azure solution is placed very thin on a cover glass, allowed to evaporate, and is smeared. A small drop of the substance to be examined is placed on a slide and the cover glass with the layer of stain is pressed on this. Bacteria, especially food bacteria of the intestine of the mouse, take on a purple-red to violet-red. Spirochetes, trichomonas, etc. are also seen.

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Flagellate Infection in Euphorbia.

*Carlos Franca, Bull. Soc. de path. exot., 15: 166, Paris, March 8, 1922.*

It is clear that the insect *Stenocephalus agilis* serves to infect euphorbia with flagellate parasites contained in its salivary glands, proboscis and intestine. These parasites are the *Leptomonas davidi*. *Stenocephalus* is probably the primitive host of *L. davidi*, in Italy, Portugal

and Switzerland. The evolutive cycle of *Leishmania donovani* in *Cimex lectularius* is analogous with that of *Leptomanas davidi* in *stenocephalus*. Both parasites have more than one host. Patton has found an inoculation lesion in kala-azar. *Leishmania donovani* has an intra-cellular phase. *Leptomanas davidi* will be studied further, especially because of the light which it is likely to throw upon kala-azar.

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**On a New Ciliate, Balantidium Blattarum, Sp. Nov., Intestinal Parasite in the Common Cockroach (Blatta Americana).**

*Ekendranath Ghosh, Parasitol., 14: 15, London, April, 1922.*

The comparative rarity of this species seems to warrant the description of the parasite found in the intestinal contents of *Blatta Americana* at Calcutta. The body is irregularly pyriform, with anterior end tapering, rounded and slightly bent to the side opposite to the peristome, and the posterior end obliquely truncated, and depressed in the middle. The peristome is small, about one-third the body in length, somewhat cylindrical and directed backwards and mediad. Along the anterior margin of the peristome is a large undulating membrane, and a row of stout cilia fringes the posterior margin. The body cilia are small and closely arranged. The endoplasm is coarsely granular and is surrounded by a distinct hyaline ectoplasm. The macronucleus is spherical, and is placed behind the peristome in the middle of the body and somewhat toward the shorter side. There is a large contractile vacuole posteriorly. The length is 0.09 mm.

The 2 genera of this species, *Balantidium* and *Balantidiopsis*, have been separately defined by various workers, but Ghosh has found that they share the same characteristics and should therefore be re-united into *Balantidium*, as Bezzemberger suggests. The present species seems to be the first described from the intestinal tract of an arthropod.

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**The Cultivation of Herpetomonas, a Parasite of Pyrrhocoris Apterous.**

*G. Franchini, Bull. Soc. de path. exot., 15: 161, Paris, March 8, 1922.*

The contents of the digestive tube, or salivary glands, of the host insect were inoculated on Nöller's solid medium. The parasites may be transferred to the NNN medium, or to rabbit-blood bouillon. They are flagellate. If grown in plates of Nöller's medium, the parasites have short flagella. Numerous and long flagella are produced by growing in the Nöller medium in tubes, or in the NNN medium.

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**Morphology of Plasmodium in a Fatal Case of Malaria.**

*A. Catanei, Bull. Soc. de path. exot., 15: 104, Paris, Feb. 8, 1922.*

Catanei reports a fatal case of malaria. The comatose patient received an intravenous injection of 1.5 gm. quinin dihydrochlorid, but

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died in a few hours without recovering consciousness. There was no autopsy. The peripheral blood, obtained before death, was almost colorless; 72% of the red cells bore malarial parasites. The latter consisted of *Plasmodium praecox*, *vivax* and *malariae*. Typical, atypical and dividing forms present are described. The forms here present show that in intense, fatal or untreated infection the morphology of the parasites may be so varied that identification may be impossible. At the approach of the host's death, the parasites take on an ameboid character. The forms so produced may be transitional forms between the several species. Interesting plates are given.

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**Studies on Inoculation of Experimental Animals with Malaria.**

*C. C. Bass, Am. J. Trop. Med., 2: 107, March, 1922.*

Two things were done by Bass in these experiments which had not previously been tried. One was to make malaria cultures from the same blood with which the inoculations were made, in order to prove that the plasmodia were viable, and the other was to make cultures of the plasmodia from the same blood used in the inoculations, in serum from the particular animals in place of the human serum usually employed in cultivating them. The object of this was to determine whether the plasmodia could grow in the presence of the serum of these animals. In 3 different sets of experiments 4 guinea-pigs, 5 rabbits and 1 monkey (*Macacus rhesus*) were inoculated twice. The blood for inoculation was obtained from hospital patients. The inoculations with blood containing *P. falciparum* were made directly into the blood stream of the experimental animals. These plasmodia were proved to be living and viable because they grew and segmented on the cultures. The animals remained apparently well, and repeated blood examinations extending beyond the incubation period of malaria in man failed to show plasmodia in any of the animals except in 1 guinea-pig twenty-four hours after the inoculation. These plasmodia did not seem to have grown although those in the corresponding culture in human serum had practically grown beyond the ring stage found in the animal. The plasmodia in cultures in serum from the different animals failed to grow, although those in the corresponding cultures in human serum grew until complete segmentation had taken place. Bass's experiments furnish additional evidence that these particular animals are resistant to human malaria and tend to support the conclusion of other workers, that they are not susceptible to infection.

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**Trypanosoma Gambiense and the Agent in Its Transmission.**

*Félix Alberto Hurtado Galtés, Rev. méd. cubana, 33: 179, Havana, March, 1922.*

Of the typical diseases, trypanosomiasis is one of the most devastating. Its exciting organism, *Trypanosoma gambiense*, is transmitted to man by the blood-sucking *Glossina palpalis*. The disease is endemic in Africa, particularly on the Guinea coast, whence it has

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spread to Cuba, where the trypanosome itself is not indigenous, Galtés examined the peripheral blood of infected subjects, to determine the periods of latency of the organism. Morphology of the trypanosome: The typical form varies in length from 8 to 20 microns, and in width from 1 to 3 microns; it is a unicellular, finely granulated organism, without chromatoplasts (cytoplasmic granulations which assume stains resembling chromatin) except in the posterior portion of the cytoplasm; it has a short flagellum, and a spherical or ovoid nucleus. The kinetonucleus is pointed, ovoid and elongated, generally situated 3 mm. from the anterior extremity. These typical trypanosomes were found in the blood of the experimental animals in great numbers ten or twelve days after inoculation. The form of the organism changed with the course of the disease. Some became elongated; the flagellum assumed an exaggerated motility, and contained chromatoplasts; bulky forms also appeared which had slow movements, undulating membranes, and which retained their characteristics longer than the long forms. Spherical forms without flagella appeared, and also filamentous, spirochetiform types.

These variations have been interpreted by different authors as transformation phases and as proofs of the polymorphism of the trypanosome. Galtés concludes that the organism goes through an evolutionary cycle in the *Glossina palpalis*, before passing in the saliva of this fly to the human host.

The organisms remain in the stomach of the *glossina* for several days, increase in number, and disappear, without producing sexual forms, although some authors distinguish masculine and feminine gametes. It seems that for the transmission of the organism certain conditions are necessary, as is the case with the gametes in malaria. The kinetogametes and trophogametes appear in the blood of the infected animals about four weeks after inoculation, remain for a short time, and disappear, giving way to a latent period during which examination of the peripheral blood remains negative. Small immune bodies are formed, which later disappear, and perhaps aid in the regeneration of the parasite. These parasites live in the blood-plasma. Some authors have described an endoglobular form, but Galtés does not accept its existence.

*Glossina palpalis*: A characteristic differentiating *glossina* from other muscidae is the fact that the females are viviparous, producing larvae which become nymphs within a few hours. They vary in size from 7 to 12 mm., are dull in color, and have a large, strong proboscis, with a bulbous base. They are found only in Africa. The most common varieties of *glossina* are: (1) *G. technoides*, (2) *G. palpalis*, (3) *G. palicera*, (4) *G. longipalpis*, (5) *G. morsitans*, (6) *G. maculata*, which may be a variety of *palpalis*. A detailed description is given of the *glossina*. The buccal portions, which are of the greatest importance in this connection, consist of the proboscis, which is straight and horizontal, the labrum, hypopharynx, and labium. The salivary ducts run along the hypopharynx. The labium ends in a pointed stylet. The life of the flies is short. The fertile females live only three or four months, and produce 6 or 8 larvae, which become nymphs in a few hours. The nymphal period is twenty-five to forty-five days, depending upon the temperature. The nymphs are very resistant to external agencies. The

larvas are deposited in a dry or semihumid region, in trees or bushes near rivers. The adults thrive in a damp climate, and their numbers decrease during the dry season. They can consume an immense amount of blood. They do not fly more than a radius of about 100 meters from their place of origin.

The Spanish Commission on Trypanosomiasis concluded: (1) Glossinas may eat young vegetables; probably this is the principal food of the males. (2) Cold-blooded vertebrates, especially crocodiles, constitute a good food and further the life of the glossina. (3) Cold-blooded vertebrates cannot, however, harbor *T. gambiense*. (4) Of the warm-blooded animals, the fowl accessible to fly-bites do not harbor *T. gambiense*. (5) Glossinas frequently feed on the blood of domestic and wild animals, which do harbor *T. gambiense*, and which therefore constitute reserves of virus during the latent stage of trypanosomiasis.

(1d—303)

(1d—303)

**Relations between Virulence and Increased Propagation of the Invading Organism (Shown in Nagana Infection of a White Mouse).**

*R. Doerr and W. Berger, Ztschr. f. Hyg. u. Infectionskr., 95: 319, Berlin, March 20, 1922.*

Nagana trypanosomes injected intraperitoneally into a white mouse first multiply in the abdominal cavity, passing after a time into the circulating blood; here they increase at a fixed rate until death of the mouse occurs. In the end stages of the infection the blood in the peripheral vessels contains an enormous number of protozoa. These findings seem to prove the existence of an infection-type, in which the relation between host and invader is reduced to an especially simple form.

A notable destruction of the parasites through humoral or cellular means of defense of the mouse organism seems not to take place. To measure the rapidity of the growth of the trypanosomes in mice in the final stages of infection the tails of the animals were cut off, the exuding blood received in small mixing pipettes (to count the red blood cells) and in dilutions of 1:100, 1:200 and 1:500 were examined in the Burker counting chamber. As diluting fluid 0.85% sodium chlorid solution, with the addition of 10% inactivated guinea-pig serum, was employed. It was shown that exitus occurred as a rule when the number of trypanosomes in a cubic centimeter of blood had reached a certain value (about 1,600,000).

The incubation and total periods of infection are dependent on the number of trypanosomes inoculated intraperitoneally. The minimal effective dose of trypanosomes appears to kill a white mouse in ten days at the latest. If in an infected mouse one makes blood tests at definite intervals of time and ascertains the number of trypanosomes per cubic centimeter one must arrive at the rate of increase.

In the Nagana strain tested, the trypanosomes obtained from one mouse increase in another previously healthy mouse, as though the individual organism were doubled. A preliminary influence on the trypanosomes by injurious agents (sodium chlorid and Ringer's solutions), affects neither their proliferation nor, in consequence, their pathogenicity so long as their ability to grow is not arrested.

One passage of the trypanosomes over a short period through the guinea-pig resulted in no distinct change in pathogenicity and rate of growth when reinjected into the white mouse. After a long continued passage through the guinea-pig (four months) and a retransference to the white mouse, the incubation period and the total duration of the infection (for the same doses) appeared lengthened. The mice died fourteen or fifteen days after inoculation. This doubling of the time was found only in the first stages of the first mouse-passage of the guinea-pig trypanosomes (up to 14.7 and 16.5 hours); the time then became irregular, reaching its minimum in the end phases of the first or during the second or third passage. For the Nagana infection in the white mouse, the conception of virulence changes completely to that of rapidity of growth. This study shows the possibility of a mathematical conception of the rapidity of propagation of trypanosomes.

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(1d—304)

(1d—304)

**A Preliminary Note on Parasites Infesting Domesticated Silver Black Foxes in Canada.**

*J. A. Allen and A. B. Wickware, Parasitol. 14:27, London, April, 1922.*

As very little literature is available on this subject, the authors publish a list of parasites found infesting silver black foxes. The protozoa include Coccidium bigeminum (*Isospora bigemina* in the small and large intestines), Acarina, Sarcoptes scabiei vulpis (on the body), Otodectes cynotis (ears and external meatus), Siphonaptera, and Ctenocephalus canis (body). The nematodes include Eucoleus aërophilum (trachea and large bronchii; eggs found constantly in trachea, esophagus and feces), Belascaris cati, Belascaris marginata, Toxascaris limbata (the 3 latter penetrate the bile duct and small intestine), Uncinaria polaris (small intestine). Trematoda included Ascocotyle longa and Echinochasmus sp. (both in small intestine).

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(1d—305)

(1d—305)

**Observations on Certain Cestodes of Rats with an Account of a New Species of Hymenolepis.**

*H. A. Baylis, Parasitol., 14: 1, London, April, 1922.*

Specimens of Hymenolepis material from rats in England were examined by Baylis. *Hymenolepis diminuta*, *H. nana fraterna* and a form *H. longior*, sp. n., closely related to *H. nana fraterna*, were found in the material. *H. murina* found in rats and the human parasite *H. nana* are constantly being confused because they bear so many characteristics in common. The general result of research while still inconclusive, tends to show that the forms occurring in man and in the rat are morphologically identical, while on physiological grounds one is justified in regarding them as distinct species, subspecies, or at least varieties.

The measurements and the morphologic characteristics of the new species, *H. longior*, are described. Some of the measurements correspond to those of *H. nana* or *H. nana fraterna*. One characteristic of  
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great importance is the lemon-shaped inner shell, with polar knobs, which is highly distinctive of the ova. The inner shell of the eggs being composed of a relatively hard, chitinous substance, is not subject to alteration by pressure or the action of reagents to the same extent as the soft parts. Many authors have given measurements of *Hymenolepis nana* and *H. murina* and it appears to the writer that, among the individuals ascribed to the latter form, some in reality belonging to the *H. longior* have frequently been included. A table is given of the measurements of all the structures of *H. nana fraterna* and *H. longior*, also a list of *Hymenolepis* found in Muridae.

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(1d—306)

(1d—306)

**A Cutaneous Nematode Infection in Monkeys.**

*Homer F. Swift, Ralph H. Boots and C. Philip Miller, Jr., J. Exper. Med., 35: 599, May 1, 1922.*

During attempts to produce acute rheumatic fever in monkeys (*Macacus rhesus*), a number of the animals were found to be infected with a nematode, presenting several types of skin lesions, subcutaneous nodules, edema about the joints, and elongated serpiginous blisters of the palms and soles. Larval forms of the nematode and possibly adult male forms were found in the subcutaneous nodules, the reaction about the worms consisting of proliferation of fixed cells, and invasion of eosinophiles, with subsequent presence of giant cells, young blood-vessels, and finally capsule formation; eventually the worms were killed and eliminated, and the nodule disappeared.

The adult female worm, it was found, burrowed into the epidermis of the palms and soles, producing an elongated serpiginous blood blister that became purulent. In this blister the eggs were laid, the bursting of the blister discharging them into the outer world, and thus placing them in a position to infect new hosts. The reaction in the epidermis was evidently not severe enough to interfere seriously with the health of the host or with the continuation of the egg-bearing period of the female parasite. This condition of almost perfect parasitism is ideal for the continuation of the life of this species of nematode. So far as could be determined this is the first description of a nematode which lays its eggs in the epidermis.

The authors give the parasite the provisional name of *Trichosoma cutaneum*, 1922, and make this report particularly for the information of other experimenters using monkeys.

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(1d—307)

(1d—307)

**Note on the Habitat and Structure of Crassicauda (Nematoda).**

*H. A. Baylis, Parasitol., 14: 9, London, April, 1922.*

Complete specimens of this nematode are difficult to obtain since the worms bury themselves in the tissues of the urogenital system of the Cetacea in which they are found. Baylis received interesting specimens of *Crassicauda* material from South Georgia accompanied by the note that the free portion of the worm varied from 2 to 4 in. in length. After traversing the fibrous tissue for some distance, the body passes into a dense nodule, where it becomes flattened and much coiled. The

substance surrounding the worm in this nodule is in some cases putty-like, in others hard and apparently calcareous. The worm eventually passes into a second nodule of pus and fibrous tissue in which the head is found. The extraction of a complete male, which proved to be *Crassicauda crassicauda*, (Crepl.) and of anterior portions of females enabled Baylis to add some further details to the description of this species.

The mouth, laterally compressed, leads into a similarly compressed buccal cavity, with very thick cuticular walls. An esophagus consists of a relatively short anterior portion, almost nonmuscular, and a very long posterior portion, which is partly muscular and partly granular. The latter portion may double upon itself several times in its course. No excretory portion has been detected. A table gives the measurements of the complete male and incomplete female. Although *Crassicauda* has been assigned tentatively to the family Filaridae, the general structure of the esophagus and buccal cavity resembles *Tetrameres*. However the globular form characteristic of the mature females of *Tetrameres* is not seen in *Crassicauda*.

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(1d—308)

(1d—308)

**An Accidental Infection with Uncinaria.**

*Fred. C. Caldwell, Parasitol., 14: 51, April, 1922.*

In the study of a method for the recovery of *Uncinaria* larvae from the soil, one of the employees of the laboratory became infected under circumstances closely simulating experimental conditions. A bottle of larvae recovered from the soil was placed on a shelf with a warning that they were not to be handled. An employee, after demonstrating a preparation of the larvae to some friends, noticed an intense itching at the tip of the thumb and base of the middle finger. The following day the 3 areas were inflamed and swollen and contained a number of minute red points, but no pus. Two days later a marked tenderness in the region of the axillary gland was observed, but no lymphangitis; the hand lesions had not changed. On the fourth day marked bronchitis developed. The lesions on the hands disappeared after thirteen days; the stool was then negative for *uncinaria*, but on the thirty-eighth day, the diagnosis was positive. Six months later he had marked symptoms of the disease, but had not taken treatment. After one course of chenopodium, repeated examinations for ova were negative, and except for palpitation of the heart the physical condition became quite good. From the history it seems certain that the larvae after passing through the skin, traveled up the lymphatics, through the axillary glands, into the blood stream and lungs in three days. The parasites reached the intestines and matured within thirty-eight days.

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(1d—309)

(1d—309)

**On the Hatching and Migration in Mammalian Host of Larvas of Ascarids Normally Parasitic in Cold-Blooded Vertebrates.**

*R. J. Ortlepp, J. Trop. Med. & Hyg., 25:97, London, April 15, 1922.*

Various workers have demonstrated that ascarid larvae, before  
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reaching maturity, have to pass through the liver and the lungs. The migration is generally believed to be by way of the blood stream. The author confirmed these results by ingestion experiments on 2 full-grown mice. The embryonated eggs of *Ophidascaris filaria* and *Polydeltphis attenuata*, mature females of both having been collected from 2 diamond pythons, were used throughout the experiments. That these results could be obtained in a warm-blooded animal with parasites from a cold-blooded vertebrate host, is very interesting, and tends to show that ascarid larvae will undergo partial development in, and produce harmful effects on a host which is only very distantly related to the normal host. Possibly the work of Asada, who claims that ascarid larvae penetrate intact skins of mice, rats and guinea-pigs, throws some light on the problem of how these larvae reach the lumen of the intestine in order to reach sexual maturity. Fülleborn supports this view, but the author was unable to obtain evidence of penetration of intact skin with unsheathed larvae of *P. attenuata*. The embryonated eggs of these parasites can withstand dryness for prolonged periods without harmful effects on the embryos. Drying also has some effect upon the subsequent hatching of the embryos. Increased heat up to 86° F. has a stimulating effect on the activity of the larvae, after that increase in temperature appears harmful. As the heating stage used does not increase temperature beyond 96° F. it was not possible to determine at what temperature the larvae are killed.

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(1d—310)

(1d—310)

**On Ascaris Vitulorum Goeze.**

*C. L. Boulenger, Parasitol., 14: 87, London, April, 1922.*

After a close microscopic study of *Ascaris vitulorum* taken from a buffalo in Punjab and from ordinary cattle in Northern Rhodesia, Boulenger found differences in several respects from *A. vitulorum* described by Neumann. A detailed account of *A. vitulorum* based solely on the material from India and Africa indicates that it does not agree with *A. vitulorum* described by Neumann in 2 of the most important specific characters, namely, the absence of cephalic papillas on the lips and postanal papillas on the male tail. The worms studied by the author have distinct papillas on the lips in much the same position as in *A. lumbricoides*, and the male specimens also have genital papillas behind the cloaca. The species described is evidently a common parasite in both localities for the sender of the material reported that the parasites were very common and when present in large numbers, caused scouring, wasting and death of the infected calves. Only sucking calves seem to be infected.

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(1d—311)

(1d—311)

**An Interesting Case of *Cysticercus Fasciolaris* Infesting the Brown Rat.**

*A. T. Hopwood, Parasitol., 14: 14, London, April, 1922.*

The infested rat measured 18 cm. in length, weighed about 275 gm., was vigorous and apparently healthy when caught, but when killed and examined, its liver was found to be heavily infested with  
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cysticerci, larvae of the common tapeworm *Taenia taeniaeformis*. On the ventral surfaces of the ventral lobes of the liver (shown in a photograph) 108 cysts were visible. The dorsal surfaces of these lobes as well as the entire surfaces of the others harbored cysts almost to their full capacity. A total of 256 larvae were visible and possibly many more were embedded in the tissue. Possibly not more than nine-tenths of the liver was incapacitated and the bile-ducts were not greatly obstructed. The identification of the cysticerci was confirmed by reference to the Zoölogical Division of the Bureau of Animal Industry of the United States Department of Agriculture.

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(1d—312)

(1d—312)

**Occurrence of *Heligmosomum brasiliense* Trav. in England.**

*G. C. Duggeon, Parasitol., 14: 13, London, April, 1922.*

In 6% of 400 rats, *H. brasiliense* was found. The rats were all of one species, *Epimys norvegicus*, and came chiefly from London and suburbs. The worms were found generally in the upper third of the small intestine. The average length of the male worm is 2.8 mm. and the width 0.087 mm. The spicule averages 0.561 mm. Bursa lobes are asymmetrical; the lateroventral and externolateral rays of the left lobe run parallel, generally contiguous, through their length. The right lobe is much thickened and normally rolled into a bar. The short dorsal lobe bears 3 rays, the central one terminating in 2 branches, which are again divided, the inner digitation bearing a small node on its outer edge, the outer digitation being slightly curved upward. The female averages 3.7 mm., with a thickness of 0.106 mm. In the median section 14 longitudinal ridges are visible; those of the lateral area are deeper and more prominent than the dorsal or ventral ones. These ridges diminish in number toward the anterior end, appear to be all present posteriorly, but of more uniform and much reduced dimensions. These measurements differ remarkably from those of the Australian specimens but the general form of the worm from both continents is the same.

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(1d—313)

(1d—313)

**Description of a Box for Collecting and Transporting Living Insects, etc.**

*E. N. Pavlovsky, Parasitol., 14: 47, London, April, 1922.*

The external dimensions of the box are: length 45 cm.; breadth 31 cm.; and depth, including thickness of lid, 5.5 cm.; internal depth, 4.6 cm. The wooden lid consists of 3 sections, each hinged, and able to be opened independently of the others. Each section is fastened by a pair of hooks screwed to the front wall of the box, suitable pins or eyelets being fixed into the edge of the lid for the hooks to engage. For greater security an additional hook is fixed at each end of the box. The interior is divided by 8 continuous fixed transverse partitions with equidistant vertical slots for the reception of quadrangular pieces of wood which divide the spaces between the continuous partitions into 6 compartments; space slots at the ends of the continuous partitions serve for the reception of the quadrangular movable partitions, when it is desired to increase the capacity of a compartment by the removal of

one of these. This divides the box into 54 compartments each measuring  $4 \times 4 \times 4.6$  cm. Double compartments made by the replacements of movable partitions are suitable for the reception of solpugids or large scorpions. Further replacements give triple capacity and by removal of all movable partitions lizards can be accommodated therein.

The lid of the box is furnished with apertures closed with corks. The floor of the box is formed of wire gauze which is made secure by a fillet of wood running around the lower edges of the box and screwed to the lateral walls. The rectangular compartment may be subdivided by the use of tin plates of suitable shape. These plates are inserted diagonally, either singularly or crosswise in pairs. The broad incision in the upper edge of each of the diagonal division plates should be cut to fit closely to the part of the cork protruding through the aperture of the lid. The writer has used the apparatus for 4 years and finds it more suitable and convenient than the generally used collection jars.

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(1d—314)

(1d—314)

**On the Larva and Pupa of a Parasitic Phorid Fly—*Hypocera incrassata* Mg.**

*Hubert M. Morris, Parasitol., 14: 70, London, April, 1922.*

Larvas of a parasitic dipterous larva, which eventually proved to be those of *Hypocera incrassata* Mg. were observed to leave the bodies of larvas of *Bibico marci*. Among the latter were noticed both unhealthy and dead forms. The larvas of *H. incrassata* pupated in the soil immediately after leaving their hosts, and only a single parasite was observed in each of the latter. This is the first definite record of an insect parasitic on Bibionid larvas.

Morris describes in detail the measurements and structures of the larvas, puparium, and the pupa; also the emergence of the adult from the puparium. A comparison of the larvas of this species with that of *Phora Bergenstammi* Mik., *P. rufipes* Mg., and *P. ruficornis* Mg., as described by Keilin, shows marked differences. The absence of sensory structures in *H. incrassata* may be an adaptation to a more completely parasitic existence, as may also be the simpler buccopharyngeal armature, with the fusion of the usual 2 mandibular sclerites into an impaired organ. The study of this larva lends support to the opinions of Brues, de Meijere, and Keilin that the position of the Phoridae in the classification of the Diptera should be among the Cyclorrhapha.

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(1d—315)

(1d—315)

**Nosema Apis and Acarapis (Tarsonemus) Woodi in Relation to Isle of Wight Bee Disease.**

*George W. Bullamore, Parasitol., 14: 53, London, April, 1922*

Bullamore gives data which shows that epidemic bee disease occurred in many countries and in some as early as 950 A. D. This disease is of great economic importance and has therefore attracted the attention of many scientists. In 1906 the bees in the Isle of Wight suffered from paralysis; the disease was given the name Isle of Wight disease. The disease usually manifested itself by the presence of num-

bers of crawling bees with their abdomens distended with undischarged feces. In a few months all the colonies in the apiary were dead.

Many attempts have been made to ascertain the cause of the disease. Many workers believe that it was due to a protozoön, *Nosema apis*, which was found in bees, but this protozoön was observed by Anderson and Rennie to be present in stocks without any disease symptoms appearing. In 1920 Rennie described a new species of mite, *Tarsonemus woodi*, from the tracheas of hive bees. The cause of the Isle of Wight disease was attributed to this mite, and the name of the disease changed to acarine disease. Hirst renamed the species of the mite *Acaparis woodi*. The mites gain entrance to the tracheas by means of the first pair of thoracic spiracles. Crawling of bees is generally followed by the death of the affected colony.

Isle of Wight disease has never been clearly shown to exist in any other country and Rennie believes that *T. woodi* is at present a parasite of bees in that island only. Bullamore states that although *T. woodi* may not be the cause of the disease the discovery of the mite is of economic importance, as it shows one of the causes of disease of modern bee-keeping. Bullamore believes that the mite will prove a comparatively harmless parasite in countries where 2 or more honey harvests and constant activity are the rule. If this opinion is confirmed the mite will be found in other countries where there is a large amount of unexplained paralysis.

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(1d—316)

(1d—316)

**Some Observations on the Biology and Structure of *Ornithodoros Savignyi*, Andouin.**

*Norman Cunliffe, Parasitol., 14: 17, London, April, 1922.*

Because of lack of details of the life cycle of *O. savignyi* and because this parasite is a potential disease carrier the publication of incomplete laboratory notes seems to be justified. Under its biology, experimental records are considered, relating to females kept at different temperatures, oviposition, longevity of the female tick, duration and number of nymphal stages at 22°, 30° and 37° C., duration and extent of engorgement and the influence of moisture on vitality and ecdysis. The dimension of the egg, and the changes of the hypostome, leg and spiracle undergone during development are described.

This study showed that the biology of *O. savignyi* is very similar to that of *O. moubata*. The females may deposit over 400 eggs, of which at least 60% may be fertile. Parthenogenetic reproduction did not occur during the course of the experiments. An increase in temperature of 8°C. (from 22°C.) decreases the longevity of the female from seven hundred and seventy-five to three hundred and fifty-eight days; an increase of 7° C. more (from 30° C.) reduces the period required for the production of third stage nymphs by 26%. At 30° C., the mean minimum periods required for metamorphosis are sixty days for males and seventy-three days for females. At 37° C. reproduction was inhibited. The results of the moisture experiments show that this is a decidedly unfavorable factor, as under this condition only 9% of the ticks matured, whereas in dry atmosphere 45% matured. The ecdysis period

was not markedly affected by the presence of moisture until after the third nymphal stage was attained, when the lack of vitality was indicated by a lengthening of this period. The changes in external anatomy undergone during development are similar to those already described for *O. moubata* (Cunliffe, *Parasitol.*, 13: 327, 1921).

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(1d—317)

**On the Dipterous Genera Passeromyia and Ornithomusca, with Notes and Bibliography on Nonpupiparous Myiodaria Parasitic on Birds.**

*M. Bezzi, Parasitol.*, 14: 29, London, April, 1922.

Besides the 2 genera mentioned in the title, Bezzi considers Protocalliphora, Philornis, Carnus, Chortophila and Neottiophilum from the standpoints of geographic distribution, ecology, and the way in which the species can be distinguished. His conclusions state that the Myiodaria living with birds show a parallelism between the grades of their parasitic adaptation and their systemic position.

*The lower forms.*—Acalypterata have saprophagous larvae, living in the nests of several orders of birds: Scansores, Passeres and Raptores. In the larval stage they feed upon decaying organic matter, while in the adult stage they are in some cases blood sucking (Carnus).

*The intermediate forms.*—Anthomyidae show 2 grades of adaptation; (a) lower forms, the larvae of which are mainly saprophagous or phytophagous (Chortophila) and which, like the Acalypterata, live in the nests upon decaying substances; (b) higher forms, the larvae of which are mainly carnivorous and have adapted themselves to 2 modes of life: (1) as subcutaneous parasites (Philornis) of Scansores, Columbae and Passeres, (2) as intermittent hematophagy, on Passeres (Passeromyia). *The higher Myiodaria.* Calliphorinae show in their larval stage the last 2 types of parasitic adaptation: (a) intermittent hematophagy (Protocalliphora) and (b) possibly a subcutaneous mode of life on Passeres only.

The adult flies of all the intermediate and higher Myiodaria are nonbloodsucking. It seems to be a rule among the Diptera that the forms with hematophagous adults have nonhematophagous larvae and vice versa. All these facts have to be taken into consideration in the study of other parasitic Myiodaria and especially the heterogeneous groups like Pupipara and Oestridae which undoubtedly are of polyphyletic origin, and are derived from lower, intermediate and higher Myiodaria.

(1d—318)

(1d—318)

**The Mallophagan Family Trimenoponidae.**

*G. F. Ferris, Parasitol.*, 14: 75, London, April, 1922.

Ferris examined for parasites the skins of mammals in the collections of the United States Museum and the Field Columbian Museum of Chicago. Three new species from South American mammals were referable to the Trimenoponidae. The morphologic characteristics of the male and female of the species of the genus *Harrisonia*, nov. (*H. uncinata*, n. sp.) and the genus *Cummingsia* nov., (*C. maculata*, n. sp., and *C. peramydis*, n. sp.) are described in detail.

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**1e. IMMUNOLOGY, SEROLOGY AND HEMATOLOGY**

(1e—425)

(1e—425)

**Transient Immunity and Lasting Immunity.**

*Alexandre Marmorek, Presse méd., 30:324, Paris, April 15, 1922.*

The duration of the state of immunity, different for each disease, depends upon the etiologic microbe, and consequently a strict relationship must exist between this duration, the nature of the pathogenic germ, and the biologic process in the organism from the time of its invasion. Between the 2 extremes, life-long immunity and no immunity at all, there are many grades of intermediate immunities of varying duration. In the diseases caused by sporozoa and spirochetes, the etiologic microbes become invisible temporarily at least. With few exceptions, the trypanosome infections leave the most durable immunity. An injection with a visible microbe does not produce a duration of immunity comparable to that produced by microscopically invisible germs.

From the known facts it is proved that the size of the pathogenic agent has an important effect on the duration of the immunity; and that the long duration of the condition of defense in certain diseases depends upon the extreme smallness of the microbe which provokes them. Observations also show that there is an intimate relation between the ultra-microscopic microbes with nuclei, and the diseases caused by ultra-microscopic agents. Such diseases must be considered, as an infection of the cellular nuclei. The study of transient immunity appears to have given all that it is capable of giving. Research in bacteriologic therapeutics, with its superb successes in the beginning, must eventually end in a sterile monotony, giving nothing but mediocre results. A new conception of immunity based upon the foregoing facts, among others, has at least the advantage of opening up fresh possibilities of research.

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(1e—426)

(1e—426)

**Experiments on the Specific Activity of the Bacteriophagus.**

*Bail and Watanabe, Wien. klin. Wchnschr., 35:362, April 20, 1922.*

The division of a natural bacteriophage into its components may be very simple, but in many cases it still proves quite a difficult test of skill. However, it is quite indispensable and necessary, not only for the purpose of correctly determining such matters as specificity and adaptation, but also because it makes it possible to differentiate, classify and systematize the bacteriophagi, which are found in great abundance.

According to the author the living and reproductive bacterial substance represents the origin and reproductive source of the bacteriophage. Bordet and Ciucu both reached the conclusion that reproduction of bacteriophagi is dependent upon bacteria, an important finding, as it proves that the living vegetative quiescent bacillus is not the basis of dissolution but only its active generative mass. The reproductive process, which may be regarded as an activity of the germinal substance of the bacteria, must set in to permit the activity of the bacteriophage, and for this reason certain reservations are necessary in designating this as "autolytic." Even though reproduction of bacteriophagi occurs

simultaneously, and though bacteriophagi may be considered as part of the bacteria, the conclusion becomes inevitable that it is not a rôle of the vegetative part, but only of the generative mass. As a matter of fact, every cell division (spermatogenesis, for instance) teaches that two things occur to the cell nucleus under the influence of the activated germinal substance (chromatin): destruction of the old nucleus and its wall and reconstruction of two new ones. That is, the activated chromatin can dissolve the vegetative part of the nucleus and, later, reconstruct the same. If it be assumed that the germinal substance (chromatin), for some reason or other, loses the second faculty but retains the power to dissolve, then something corresponding to the bacteriophagus would result.

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(1e—427)

(1e—427)

**A New Method of Demonstrating d'Hérelle's Virus.**

*Pfreimbter, Sell and Pistorius, Münch. med. Wochenschr., 69:495, April 7, 1922.*

The author has succeeded in demonstrating the action of d'Hérelle's virus in all representatives of the typhoid-dysentery-colon bacillus group. They found the virus in 9 different cases, in the excrement of normal individuals, in patients, bacillus carriers and in an old culture of Y-dysentery bacilli. In demonstrating d'Hérelle's phenomenon the chief part has heretofore been played by the clearing up of turbid emulsions of bacteria. In the authors' studies this method has proved unreliable; the action of d'Hérelle's virus could be demonstrated in bacterial suspensions that remained turbid. Therefore the clearing up of bacterial emulsions is not a reliable method and may even lead to mistakes. Among the other methods that have been proposed the authors prefer that of implanting on agar plates suspensions of bacteria that have been inoculated with d'Hérelle's virus. They found in the colonies the round holes that have been described by d'Hérelle, and also Gildemeister's "Flatterformen." The plate method is more reliable than d'Hérelle's method, and also promises important information as to the nature of the processes underlying d'Hérelle's phenomenon.

The author recommends the following method for demonstrating the virus: (1) the addition of a small amount of the virus to a dilute bacterial emulsion; (2) sowing this on an agar plate (*a*) immediately after the addition of the virus and incubation, (*b*) after three hours, (*c*) after six hours and (*d*) after twenty-four hours. If after three hours no further growth is to be seen on the plate the virus is highly virulent and the experiment of making plates should be repeated at shorter intervals. If the action of the virus is slight the observation should be continued for longer than twenty-four hours. By this method was tested the action of 7 species of virus on 14 strains of the typhoid-dysentery-colon bacillus group resulting in 58 positive reactions. Clearing up of a suspension occurred in only 38 of these cases. It was sometimes of short duration and in several cases was uncertain. This gives a superiority of 52.6% for the plate method; moreover the observation by this method is much more objective than by the other.

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**The Nature of d'Hérelle's Bacteriophagus.**

*R. Otto and W. F. Winkler, Deutsch. med. Wchnschr., 48: 383, Berlin, March 24, 1922.*

Opinion is still divided as to the nature of d'Hérelle's principle, which is injurious to bacteria, and filtrable and autolytic. This principle had been previously demonstrated by Twort. D'Hérelle's phenomenon is supposed to be due to the fermentative effect of extremely small bacteria which appear when the original bacteria die. The authors attempted to determine the nature of these bacteriophagi. The appearance of the bacteriophagus lysin may be favored by various procedures. In the production of the virus there is a special importance in the filtration through a bacterial filter. This allows an especially effective colloidal solution of the very small bacteria while the larger particles are excluded. These larger particles may be the ones which absorb some of the characteristics of the smaller ones.

Experiments were also performed with complement formation. These show that the lysin which is closely associated with the very small bacteria is a specific and noncongruous antigen in relation to the bacterial albumen which acts as an antigen and which results from the killed larger bacteria. It greatly resembles the structure of the autolysate of live bacteria. The antilysin has antilytic bodies and also a specific quota of Bordet's antibodies against the lysin. The results are not conclusive in showing that there are special invisible bacteria. There is some reason to believe, however, that the active agent in d'Hérelle's phenomenon may be in the nature of fine albuminous particles of the bacteria with fermentative qualities which are formed on the disintegration of the live cell.

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**Origin of the Phagocytes of the Lungs.**

*Heinrich Westhues, Beitr. z. path. Anat., etc., 70: 223, Jena, March 11, 1922.*

To learn the origin of the phagocytes of the lungs, the author injected carmin under the skin of rabbits and India ink into the veins. Then he injected concentrated cultures of tubercle bacilli into the veins; but the cultures were not virulent enough to cause the formation of tubercles. Results showed that the entire reticulo-endothelial apparatus was so filled with lampblack that there was no place for the hoarding of carmin. Modifications of the experiment seemed at first to permit the conclusions that: (1) histiocytes in the lungs are extremely few in number; and (2) these histiocytes play no part in the formation of epithelioid cells, especially as the epithelioid cells did not show granules of carmin. Afterward colored compounds were dropped into the trachea of guinea-pigs, by a tracheotomic wound and through this channel into the lung. These experiments showed that histiocytes are in the lungs in far larger numbers than has been hitherto admitted; further, that phagocytosis occurs in the lung more powerfully and energetically than the histiocytes can perform phagocytosis so that the consumed cells found in the alveoli are not migrated tissue cells, but merely alveolar epithelium. Finally, these experiments show that the

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potent phagocytosis inhibits the function of the cells (cells filled with lampblack cannot admit carmin in form of granules) and that also the vitality of the cells is lowered, because the imbibition of carmin persists to a large extent in the nuclei of these cells.

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**The Effect of Peptone on the Toxigenic Property of *B. Diphtheriae* No. 8.**

*Harriet Leslie Wilcox, J. Infect. Dis., 30: 536, May, 1922.*

The No. 8 strain of *B. diphtheriae*, isolated in 1895 and used both here and abroad in obtaining a potent toxin, had appeared to have stable toxigenic properties until 1914, when irregularities in the strength of the toxin were noticed. Recently the strain which had been taken to the Pasteur Institute in Paris in 1896, where it had been under cultivation on Martin peptone broth, was brought to this country and cultivated on Witte peptone broth. At the same time the New York strain which had been cultivated on Witte peptone broth was transferred to Martin peptone broth and comparative tests were made. From the findings, Wilcox reaches the conclusion that Witte peptone broth has an inhibitory or destructive influence on the toxigenic powers of both cultures, and that the different preparations of Witte peptone received in this country just prior to 1914 may be responsible for this deleterious effect. The fact that culture Research No. 8 from the time of its isolation in 1895 to about 1914 had been cultivated in Witte peptone broth without any signs of the lowering of its toxigenic property, as shown by the production of a potent toxin, tends to confirm this last conclusion. It is possible that the different preparations of any peptone may vary in their effects on the toxigenic property of *B. diphtheriae* No. 8. That continuous cultivation of a culture of *B. diphtheriae* No. 8 in the same broth as that used for toxin production is apparently not necessary for obtaining potent toxin, is shown by the American strain of No. 8, which after only 7 generations in Parke-Davis broth gave as potent a toxin in that medium as Pasteur No. 8 which had been cultivated for eleven months in Parke-Davis broth.

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**Observations on the Preparation of Toxin-Antitoxin Mixture.**

*P. G. Heineman and Charles R. Hixson, J. Infect. Dis., 30:508, May, 1922.*

Immunization against diphtheria by toxin-antitoxin has been successful, but depends on the proper balance of the toxin and antitoxin. The mixture should contain a slight excess of toxin; a completely neutralized mixture has less immunizing value than one which is slightly toxic, and a mixture with an excess of antitoxin is of still less value.

The authors review the directions for the preparation of toxin-antitoxin as set forth by the Hygienic Laboratory, which have, however, been slightly changed since the paper was prepared, and give the results of their own experience. Their work was based on the assumptions that Erhlich's theory that the toxin molecule is made up of prototoxoid

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(nontoxic), toxin, and toxone (causing paralysis) is correct; that anti-toxin has an avidity for prototoxoid, toxin, and toxone, in the order named; that the combination between prototoxoid and antitoxin is relatively firm as compared with the combination between toxin or toxone and antitoxin; that the combinations in the latter case are slow as compared with chemical processes, and that all toxins are not entirely homogeneous.

Mixtures which give satisfactory tests occasionally increase in toxicity later, showing that great care in preparation is necessary, and that toxins should be well ripened. If the excess toxin is too large severe local or septicemic reactions may occur. The greatest safeguard is the allowance of sufficient time in the preparation.

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**Preliminary Experiments with a View to the Preparation of a Nontoxic Dysentery Vaccine.**

*F. R. Coppinger and R. C. Robertson, J. Roy. Army M. Corps, 38: 243, London, April, 1922.*

If any method can be devised which will diminish the toxic properties of the dysentery bacillus without affecting its antigenic value as a vaccine, considerable advance will be made in the possibilities of vaccine prophylaxis. The experiments described in this paper refer only to the Shiga bacillus, but as this organism is by far the most toxic of this group, it is considered that if its toxicity can be reduced without affecting its antigenic properties, little difficulty would be experienced with the other organisms of the group. A method for reducing the toxicity of the Shiga bacilli by treating them with NaOH, neutralizing with HCl, and precipitating with alcohol, appeared to be fairly satisfactory. In view of the amount of alcohol required it was considered desirable to try some more economical method of preparation. According to the procedure adopted a mixture of equal parts of a thick emulsion of Shiga bacilli and liquor ammoniae fortis (B. P.) was allowed to stand in the incubator at 37°C. over night. Neutralization was then effected by means of 20% sulphuric acid, which, combined with ammonia, formed ammonium sulphate. No precipitation occurred until the neutral point was reached, when a heavy precipitate immediately formed which rapidly subsided to the bottom of the flask leaving a clear supernatant fluid. When the precipitate was separated and washed it was found to be composed of bacilli which were somewhat swollen and altered in shape, but still quite discrete and distinct. Inoculation into rabbits showed that these altered bacilli were relatively nontoxic but retained their antigenic properties. Whether vaccines prepared on the same lines would be satisfactory for the prophylactic or therapeutic treatment of bacillary dysentery in human beings has yet to be proved.

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**On the Action of Sodium Citrate on the Phagocytosis of a Bacillus Influenzae.**

*Susumu Amaya, Japan Med. World, 2: 106, Tokio, April 15, 1922.*

It has been found that certain salts inhibit phagocytosis, but that  
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very dilute solutions of certain salts stimulate it. Sodium citrate inhibits the action of phagocytic complement. The phagocytic power of normal rabbit plasma against *B. influenzae* is not inhibited by 1.4-1.56% sodium citrate concentration; it is markedly inhibited by 1.9%, and with a concentration of 2.23-2.56% the percentage of phagocytic leukocytosis is reduced about 10%, and spontaneous phagocytosis is almost entirely abolished. The phagocytic power of an immunized rabbit blood plasma, however, is still strong.

Agglutination shows a distinctly positive result within a certain period of time, but after a certain time, spontaneous agglutination occurs and the result is not reliable. The complement fixation tests give distinctly positive results. The phagocytic tests with *B. influenzae* and a certain large amount of sodium citrate is more reliable than the agglutination test and the accuracy of the results of phagocytic tests with this method is about equal to that of the complement fixation tests. Therefore this method of phagocytic test has a certain value as a specific immunity reaction.

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**Toxicogenic Power of Pfeiffer's Bacillus.**

*B. Gosio and A. Missiroli, Ann. d'igiene, 32: 6, Rome, Jan., 1922.*

By means of types of Pfeiffer's bacillus isolated in the epidemic of 1919, it has been possible to produce in guinea-pigs a remarkable set of phenomena based upon congestive, hemorrhagic, and inflammatory action, with striking preference for the lungs and the lymphatic glands. The various types all possess this pathogenic activity, in which the dominating element is the toxin of the bacterial cell, usually without any aggressive power on the part of the bacteria themselves, which are differentiated only by their diverse toxicogenic energy. Toxic phenomena causing death may appear many days (eight to ten) after inoculation with the virus. Hence there may be a period of more than a week during which the organ is under the influence of toxin without the possibility of immunization. This fact should be remembered in the use of bacterial vaccines into which the Pfeiffer bacillus enters as a part. Besides the genuine Pfeiffer's bacilli, other microorganisms which share some of their characteristics may be isolated from cases clinically diagnosed as influenza. These are, however, distinguished by their biologic properties and by their different pathogenic action on susceptible animals. There is still some question as to whether the importance of Pfeiffer's bacillus is absolute or only relative. The authors maintain that the Pfeiffer bacillus is sufficient to explain the etiology of influenza, but this does not mean that it is necessary. It would in fact be difficult to combat the opinion of certain other investigators who believe that there is still another bacterium which prepares the way for Pfeiffer's bacillus. The same question may be put concerning many other pathogenic bacteria.

These conclusions are based upon the authors' studies made up to February, 1919. Having later extended their researches, they combat the assertion of other investigators who declare that influenza is too difusible to admit of being produced by a schizomycete. They affirm that the form, dimensions and physical characteristics of the virus are secondary matters when other factors of great importance enter, such as the

easy and abundant spread of the infectious material, the ready access of this material to the respiratory mucosa, and man's extreme susceptibility to the infection. The assumption that a virus is filtrable simply upon the ground that it is diffusible is not strictly in accordance with logic. Exposing individuals to vaporization of liquid rich in Pfeiffer's bacilli or to their introduction either subcutaneously or in the cavity of the nose did not produce results in proportion to the contagiousness of the disease. Now, these results looked at in their extreme practical consequences would indicate that the disease was not contagious; it is more logical, however, to conclude that in the above experiments the effect of some modifying circumstance prevailed (antagonistic microbic flora?) which interfered with the infection. On the other hand, it is necessary to admit the variety of the bacteria. It is easy to isolate hypertoxic forms of influenza bacilli while the epidemic is at its height. Even Pfeiffer worked on attenuated forms two years after the epidemic of 1889-90.

The various types of Pfeiffer's bacillus agglutinate differently. Other investigations suggest the important idea that agglutinability in general (*ceteris paribus*) varies from strain to strain and that it would be useful to precede attempts at diagnosis with a choice tending to identify the varieties best fitted for the purpose. There is need of further study in this direction for the purpose of defining, upon the basis of widespread and close observation, all points regarding the appearance of agglutinins in the blood of the patients, their duration, and the most opportune moment for identifying them in their maximum quantity. The cutaneous reaction practiced upon infants within the first thirty-six hours after the attack of influenza with various types of Pfeiffer's bacillus has given results of considerable diagnostic importance.

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**Preparation of an Antiinfluenza Serum.**

*B. Gosio, Ann. d'igiene, 32: 58, Rome, Jan., 1922.*

Horses and other large animals, were used for the purpose of obtaining large quantities of immune serum. The methods followed were almost the same as those adopted for antistreptococcic, antimeningococcic, and antidysenteric serum. Gosio had at his disposal many well-identified types coming from different regions. He began with slight subcutaneous doses calculated upon the susceptibility of guinea-pigs and in proportion to the weight of the horses (2 loopfuls of dead culture for each type); when the reactive phenomena had disappeared, he increased the dose little by little, until finally he began to inject the live colonies, first subcutaneously and then into the jugular vein. Still proceeding somewhat cautiously, he arrived at very considerable doses (30 or more colonies) without encountering any difficulty. The injections were all well tolerated, or at the most with ephemeral collapse, and never with the loss of an animal. Generally, after a period varying from three to four months, the horse attained a sufficient degree of immunity. Gosio waited another ten days, however, to be certain of the complete disappearance of the toxin from the circulation before bleeding.

The production of anti-Pfeiffer serum appears to be a process free from difficulties and of assured success, except so far as concerns the unknown character of the individual types of bacteria chosen to produce the culture. Only two conditions are necessary for the effectiveness of the serum, that of being able to employ in due time fresh and abundant cultures, and that of possessing types of bacteria of great toxicogenic energy. The first condition, being a matter of technic, may be met without difficulty by the bacteriologist; the second is dependent upon the time at which he is working. It is quite simple to isolate hypertoxicogenic varieties of Pfeiffer's bacillus during a pandemic of considerable importance; but they are rarer or absent in minor epidemics. In fact, the Pfeiffer varieties which may be isolated in recurrent epidemics, while typical as far as concerns other characteristics, differ from those of widespread pandemics in their lower toxicity. This toxicity may be increased by the use of laboratory methods, but, even so, it becomes considerably attenuated after a short time. This fact explains the slight results thus far obtained with anti-influenza serum. Concerning the practical efficacy of the serum, it was seen that guinea-pigs intoxicated by means of Pfeiffer's bacillus may be saved from death while those under control succumb. This fact constitutes the basis for therapeutic treatment by this method.

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**The Proteolytic Enzyme of *Bacillus Pyocyanus*: The Inhibition Produced by Normal and Immune Serum.**

*C. E. Dukes, J. Path. & Bacteriol., 25: 258, Edinburgh, April, 1922.*

The first example of an anti-enzyme was described by Hilderbrandt (1893) who demonstrated that the serum of animals repeatedly injected with emulsion inhibited the action of emulsion on glucosides. The question is of some interest from 2 points of view: (1) If real antibodies to enzymes are formed by the body, the view is supported that enzymes belong to that class of complex native proteins which generally excite the production of anti-bodies and with which, incidentally, enzyme preparations are commonly contaminated. (2) It is natural to suppose that in the initial stage of an infection it is the enzymes of the invading organism that enable it to derive energy and nourishment from its new environment. Dukes has attempted to answer the question whether active resistance to these enzymes form an important part of the reaction against infection.

As antigens the following preparations of *B. pyocyanus* were used: (a) suspension in saline, killed by heating one hour at 60°C.; (b) filtrate of a week-old broth culture; (c) broth culture heated to 75°C. for three hours, devoid of proteolytic activity; (d) suspension of fibrin on to which pyocynase had been adsorbed; (e) a preparation of enzyme purified by precipitating a broth culture with 4 volumes of absolute alcohol, reprecipitating the filtrate with 7 volumes of a 2:1 alcohol ether mixture, and dissolving the precipitate in dilute sodium carbonate. With the various protein tests this solution contained relatively little protein, but gave a faint turbidity with excess of absolute alcohol. The enzyme solution was prepared for all the tests by inoculating 500 c.c. nutrient broth with a well-marked proteolytic strain of

B. pyocyaneus and allowing it to grow for seven days at 37°C., the flask being shaken every day to break the surface film. It was then filtered through a Berkefeld filter and the sterile filtrate preserved in the ice-chest. A few drops of chloroform were added.

The inhibitory action of sera was measured in 3 different ways: (1) by the influence of enzyme serum mixtures on setting of gelatine; (2) by the influence of enzyme serum mixtures on the time taken to cause complete liquefaction of a unit of gelatine; (3) by the influence of sera on the rate of hydrolysis of gelatine as measured by the production of amino-acids. By a study of tables showing the results it appears that although the presence in the immune serum of an anti ferment, seemed indicated by the first method, this hypothetical antibody did not betray its presence when the second method was used. Sörensen's method also gave negative results. A resurvey of the sera exhibiting these contradictory properties showed a definite relationship between the precipitin reaction and the capacity of increasing the inhibitory titer of the serum as tested by the gelatine liquefying test. The immune sera agglutinated B. pyocyaneus in titers above 1:1000. On testing for precipitins the writer found that those sera which showed apparent inhibition with the gelatine liquefaction method also gave marked reactions. Moreover, a quantitative relationship was observed to exist. When one volume of enzyme solution diluted 1:5 was floated on to one volume of serum and the tubes incubated an hour at 37°C. the following results were obtained with the 5 antigens mentioned above: Serum from rabbit injected with a, b, and c, gave a precipitin result of +++; with d,—; with e, +.

These results harmonized with the inhibitory titer which had been found to stand at 5 c.mm. with the first 3 and at 6 c.mm. with the purified enzyme, whereas, by the injection with fibrin on to which the enzyme had been adsorbed no increase in inhibition could be obtained and the titer stood at the original level of 8 c.mm. This point was investigated still further by inoculating a rabbit with a crude broth culture of B. pyocyaneus and the rabbit's blood tested for the presence of gelatine inhibition and the precipitin reaction at intervals during the course of injection. It was found that not until the precipitin reaction began to appear was there any trace of increased inhibition by the gelatine liquefaction method, and that when the precipitin reaction became strongly marked, the antagonistic action of the serum reached its maximum. The writer concludes that antifermen are produced against the proteolytic enzymes of B. pyocyaneus. The inhibition found in immune serum by the described methods of testing appears to be due to the action of a precipitin.

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#### Immunity to Tuberculosis in Guinea-Pigs.

H. Selter, *Ztschr. f. Hyg. u. Infektionskr.*, 25: 159, Berlin, Feb. 10, 1922.

Selter attempted to produce a chronic form of tuberculosis in guinea-pigs, by means of mildly virulent but active bacilli, and to determine the extent of the immunity of these animals to reinfection with virulent ba-  
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cilli. The results for 1918-1919 contribute some facts of value in the experimental study of tuberculosis. The guinea-pigs were injected subcutaneously, intraperitoneally, and intravenously, with varying doses of bacilli. After approximately eight to fourteen weeks they were reinfected, with the same strain of bacilli. The results demonstrated that animals which had been infected with small quantities of mild cultures (weakened by incubation for several weeks) developed mild organic tuberculosis in from four to six months, and a severe form in from eight to ten months. This ran a chronic course and developed in the animals complete immunity against reinfection of mild virulence. Injections of large numbers of bacilli—one million, for instance—for the reinfection, produced local reactions (abscesses); the organic tuberculosis was easily influenced. When small numbers of bacilli were employed, the first injection was occasionally without result. The animals succumbed to the reinfection, as no immunity was produced. Animals which had been vaccinated with Friedmann's bacilli (from cold-blooded animals) developed no immunity against reinfection with human tubercle bacilli; on the contrary, the subsequent organic tuberculosis was severe. The inference is that the preliminary treatment with Friedmann bacilli was directly injurious.

In general, the result of any reinfection, following preliminary inoculation, varies widely as regards the curative effect. It depends upon the stage of the disease which the animal presents. Selter prepared so-called vital tuberculin by triturating old cultures in an agate mortar. In addition to isolated living bacilli, this contained the bodies of dead bacilli, the sheaths of which had cracked. Animals which had been previously treated with this tuberculin from cold-blooded organisms presented the greatest degree of immunity; this vaccine also readily produced mild chronic tuberculosis. On the basis of these experiments Selter concluded that the first infection leads to the formation of ferment in the body which cause the destruction of the reinjected bacilli. The chemicophysical (not morphologic) change in the cells, which react to the irritative substance by inflammation, has for its purpose the protection of the cell from the living bacillus and its toxins. The allergy is produced only by the action of the living organisms, and does not disappear as long as living bacilli are present in the body. It may be maintained by tuberculosis or by any other irritative substances.

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**Studies on the Effects of Tuberculin. Experiments with Complement-Binding.**

*Peter M. Holst, Tubercle, 3: 289, London, April, 1922.*

A series of experiments were made with serums from rabbits, guinea-pigs and human beings. The object was not to determine the quantity of complement-binding antibodies in tuberculous serums, but to investigate the nature of their alexins and of combinations with antigens and antibodies. The serums belonged to all sorts of persons, young and old, sick and well. The amount of serum was found to be constant within certain limits. No relation could be found between the state of health of the donor of the blood and the quantity of the complement in his serum. The experiments demonstrated that what is called an alexin

or complement is not an identical substance in all serums: thus the complement in rabbit's serum differs constitutionally from that of the human being, supporting Ehrlich's view that there is a plurality of complements. The difference between the binding of rabbit's complement and human complement can be demonstrated between other heterologous serums, e. g. between the complement of rabbit and guinea-pig. This difference Holst ascribes to the circumstance that one complement is able to make combinations which other complements cannot. These combinations may arise either between specific tuberculous components of the antigen (tuberculin) and the corresponding amboceptors, or between nonspecific components and corresponding accidental amboceptors.

The experiments with human serums were divided into 2 groups: those with complement derived from persons whose relation to tuberculosis was unknown, and those with complement derived from tuberculous persons. Of 182 serums belonging to the first category only 12 differed. Thirty-five serums from tuberculous persons showed a distinct difference when compared with 207 from nontuberculous individuals, whereas no difference could be demonstrated in 86 cases. In some cases the hemolysis was more complete in the tubes with non-tuberculous complement, in others it was more complete in those containing tuberculous complement. However, a striking conformity could be observed, and the bindings of tuberculous complements in many cases were absolutely parallel.

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**The Action of Killed Tubercl Bacilli.**

*H. Selter, Ztschr. f. Hyg. u. Infektionskr., 95: 233, Berlin, Feb. 10, 1922.*

The following technic was used in the study of immunity due to preliminary treatment with killed tubercle bacilli: Guinea-pigs were vaccinated with: (1) tubercle bacilli killed with lactic acid; (2) vital tuberculin (old cultures pulverized in an agate mortar), in which any surviving bacilli had been killed by carbolic acid; and (3) vital tuberculin which had been digested with pepsin or trypsin. The reinfection dose was 500,000 living bacilli. All the experiments gave negative results, i. e., the animals which had received preliminary treatment reacted as did the controls—no immunity was produced by previous vaccination with killed bacilli. The second problem was to determine whether or not it was possible to produce sensitivity to tuberculin, by means of preliminary treatment with bacilli killed with lactic acid, or with vital tuberculin in which all the surviving bacilli had been destroyed by means of chloroform or carbolic acid. The animals which had received preliminary treatment were injected subcutaneously and intravenously after not less than thirty-two days, with old tuberculin. The intracutaneous test was constantly negative; some of the animals which had been given intravenous injections presented anaphylaxis for protein, and hypersensitivity to tuberculin. The conclusion is reached that killed tubercle bacilli are not capable of producing, in healthy animals, any manifestations of immunity which are of value in the study of immunity in tuberculosis.

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**The Action of Tuberculous Toxins.**

*Felix E. Fernandez, Cron. med.-quir. de la Habana, 48: 504, March, 1922.*

Experiments were performed to determine whether or not the serum of guinea-pigs possesses immunizing properties against the Koch bacillus. A guinea-pig was treated every nine days with 4 hypodermic injections of 0.5, 1.0, 2.0, and 3.0 c.c. of an emulsion of Koch's bacillus in 8 c.c. physiologic saline solution heated to 90°C. for half an hour. The four injections were given on two successive days. The reaction was tested by the leukocyte count and Arneth's index. Blood was drawn thirty days later, and serum obtained. An emulsion of this serum, in varying doses, was injected into 6 guinea-pigs in conjunction with Koch bacilli in saline solution. Three days later blood tests were taken. The Arneth index had risen. Three of the animals died. Autopsy revealed infiltration of the inguinal and sacral glands; the liver, spleen and lungs contained small tubercles; the suprarenal glands were completely degenerated. Apparently the serum inhibited the defences of the body, and produced marked diminution of the polynuclears. Further experiments demonstrated that the filtrated residue of centrifugalized and killed Koch bacilli, injected into guinea-pigs, produced a marked change in the leukocyte count.

The experiments are not conclusive, but seem to indicate that the soluble toxins of the Koch bacillus prepare the way for the attack of the microorganism, by means of a lowered resistance produced by an intermediary agent, a ferment; the toxins cause the destruction of the cells with which they come in contact, forming tubercles.

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**The Bactericidal Action upon Calf Lymph of Certain Triphenyl-carbinol Dyes and Their Leuko-Compounds: Immunity and Hypersensitiveness toward Vaccinia Variolae.**

*M. Copans, J. Path. & Bacteriol., 25: 173, Edinburgh, April, 1922.*

The rapid preparation on a large scale of calf lymph vaccine free from bacterial contamination and still of full potency is beset by many initial difficulties. Many investigators have obtained promising results with the use of triphenylcarbinol dyestuffs, but in the end they proved unsatisfactory. A method of preparing a bacteria-free calf lymph in from five to fifteen days is briefly as follows: To a stock mixture containing pure neutral glycerin 50.0 parts by weight, phenol, 0.5 parts, NaCl, 0.8 parts and distilled water, 50.0 parts, is added (to 4 times the weight of this stock mixture) an emulsion of vaccine pulp which has been so ground and emulsified that it is of the consistency of condensed milk. To this is added 1% of a stock solution of either 1% malachite green or 1% brilliant green made up in distilled water, and stirred immediately. A blue-green color should result. The lymph is then distributed into cylindric tubes with an air space at the top and corked tightly. After three days' incubation at 37°C., followed by seven days' at 18°C., sterility is determined. Upon the completion of the bactericidal process the dyestuff present in the emulsion is converted into the

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colorless leukocompound by treatment with sodium hyposulphite and the original natural color of the lymph becomes restored. The potency of such a treated lymph has remained unimpaired during a period of fifteen months' storage at a temperature of not less than 45° F. Before treatment with the reducing agent the dyestuffs in the concentrations mentioned are both bactericidal and vaccinicidal; the former activities may be greatly reduced and the latter practically arrested by the conversion of the first solution into the second. All potency tests were carried out on children previously unvaccinated.

A series of tests were carried out on rabbits to ascertain the extent to which inoculated animals will tolerate the effect of intraperitoneal injection of the fully potent lymph and the degree of immunity attained, as shown by nonsusceptibility to subsequent vaccination of the cornea. It was found that the intraperitoneal inoculation of calf lymph conferred durable immunity to subsequent vaccination of the cornea, and it was evident that the leukobrilliant green, in the proportion of 1/10,000, was without toxic effect, 0.5 of this substance being present in the maximum dose employed. Similar experiments were carried out in a series of 33 cases in man, the dose of the fully potent bacteria-free calf lymph vaccine, suitably diluted, varied from 0.01 to 0.02 c.c. of the emulsion. This dose given subcutaneously gave rise to a reaction which, with one exception, was entirely local in character and was free from general or constitutional disturbance. The cases fall into 2 groups, as shown by the effects of the injections. Group 1 consists of 4 individuals previously unvaccinated. The period of incubation lasted from five to ten days before symptoms of reaction were manifested. The second group numbered 29 cases, all showing cicatrices of previous vaccination or revaccination. In this case the latent period was about six hours. In both groups the symptoms of reaction were at their maximum forty-eight hours after their onset, and commenced to abate on the third day, disappearing completely by the fifth and sixth days, with the exception of a small cutaneous nodule localized at the immediate site of the puncture, which may persist for ten days or more. If Coplans' method of preparation of the lymph and technic of injection are followed, danger of sepsis will be eliminated. The series of 19 cases include 2 vaccinated three and seven and a half years previously. By excluding the latter, the result is that out of a total of 76 scarified areas inoculated subsequent to subcutaneous injection, only two yielded abortive vaccinal eruptions, whereas the 28 scarified areas in 7 control cases, previously unvaccinated and uninjected, yielded 28 typical vaccinal eruptions.

The gain in time of the incubation period of persons previously vaccinated or revaccinated is presumably of material importance in relation to the question of urgent protection of such persons when exposed to the danger of infection from smallpox. Three cases are described in detail in which continued refractoriness to vaccination or revaccination is associated with an intense degree of supersensitivity on subcutaneous injection of the vaccine virus. While these 3 cases gave a clear history of earlier nonsusceptibility to vaccination or revaccination, such refractoriness is not necessarily associated with supersensitivity. Coplans states that the general validity of the method of subcutaneous injection of pure and potent vaccine virus, to replace that

of vaccination by skin scarification with its attendant dangers from sepsis, can only be determined as the result of more extended observations, but he quotes Ricketts and Byles to the effect that if a person has been shown to be really insusceptible to vaccinia, that fact is proof positive that he is insusceptible to smallpox.

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**Does Preventive Inoculation Cause Immunity to Foot-and-Mouth Disease in Cattle and Guinea-Pigs?**

*P. Uhlenhuth and W. Bieber, Klin. Wchsnchr., 1:734, Berlin, April 8, 1922.*

In 1898 the Prussian commission for the study of foot-and-mouth disease decided that preventive inoculation does not protect against the disease. To test the question further 3 calves that had been immunized to a high degree were put in an infected stall with a number of animals that had the disease; they did not develop any symptoms in six weeks. In analogous experiments with other immunized animals all the animals put in the infected stalls had the disease, though only in a mild form. The question of the mutual immunity produced by vaccination and by foot-and-mouth disease was further studied in guinea-pigs. After vaccination, symptoms similar to those of foot-and-mouth disease developed on the skin, but the pustules appeared later and were limited to the site of injection, while the vesicles of foot-and-mouth disease extended to the toes. Guinea-pigs could be completely immunized to vaccine, but on later infection with the virus of foot-and-mouth disease they had the disease almost as severely as nonimmunized control animals. On the other hand, guinea-pigs immunized to foot-and-mouth disease were infected with vaccine and had pustules like the control animals. The experiments did not show any mutual immunization by vaccine and foot-and-mouth disease virus.

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**Heat and Growth-Inhibiting Action of Serum.**

*Alexis Carrel and Albert H. Ebeling, J. Exper. Med., 35:647, May 1, 1922.*

Plasma or serum from an adult animal possesses an inhibiting power on the growth of a pure culture of homologous fibroblasts, and it is evident that if this power is as marked *in vivo* as it is *in vitro* it must play an important rôle in many physiologic and morbid processes. Carrel and Ebeling have, therefore, carried on an investigation into its nature, and in the present paper report their study of the modifications occurring in the rate of growth of fibroblasts when the serum composing the culture has been heated at various temperatures. The serum used was obtained from chicken plasma. It was found that the inhibiting action of homologous serum on the proliferation of fibroblasts *in vitro* was increased 15% after the serum had been heated at 56°C. and 34% after it had been heated at 70°C., but was decreased after heating at 100°C. This increase is considered to be due to the production, under the influence of heat, of a change which renders the

serum more toxic for the homologous fibroblasts; or to the destruction of cells presenting the same heat resistance as complement and amboceptor, and partly protecting the cells against the inhibiting action of a third substance resisting heat at 70°C. Serum modified by heat acts in an opposite manner on heterologous tissues.

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**Surface Tension of Serum. II. Action of Time on the Surface Tension of Serum Solutions.**

*P. Lecomte du Noüy, J. Exper. Med., 35: 707, May 1, 1922.*

Having previously shown that the surface tension of serum decreased rapidly on exposure to the air, du Noüy measured the surface tensions of the same samples at different intervals, ranging from two minutes to twenty-four hours, in order to determine the effect of time. He found that in serum diluted to as low as 1:1,000,000 in physiologic saline solution, the surface tension of the liquid is lowered by 3 or 4 dynes in two hours; at 1:100,000, by about 11 dynes (mean value) in two hours, and by 20 dynes in twenty-four hours; at 1:10,000 by about 13 to 16 dynes in two hours. The drop in surface tension is much more rapid in the first thirty minutes, and follows generally the law of adsorption in the surface layer in function of the time. Stirring or shaking after the drop causes the surface tension to rise, but generally to less than its initial value. With sodium oleate, glycocholate, or saponin instead of serum, the same phenomena occur. For every serum, as well as for the substances mentioned, a maximum drop occurs in certain conditions at a given optimum concentration. Not only are the substances which lower the surface tension adsorbed in the surface layer, but also the crystalloids themselves. This is plainly shown by the evaporation of such solutions in watch glasses, which leaves, instead of a small group of sharp, large, well defined crystals at the bottom, a white disk almost as large as the initial free surface itself, due to the liberation of the salt by the surface layer as it crawls down the concave surface of the glass. In these conditions, solutions of serum are characterized by a very peculiar periodic and concentric distribution of the crystals, at a concentration of 1:100 only. The same ring-like aspect is observed with sodium oleate, glycocholate, and saponin, but not at the same concentration, as was to be expected, since serum is a solution in itself.

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**The Transmission of Complement-Fixing Substances from Mother to Child.**

*J. V. Cooke, Am. Rev. Tuberc., 6: 127, April, 1922.*

The transmission of specific immune bodies from the mother to the young has been studied experimentally by a number of investigators, and specific antitoxins, lysins, agglutinins, opsonins and complement-fixing antibodies have been found in the offspring of immune mothers, although some of the results are conflicting. As a rule the immune substances in the offspring are less in amount than in the mother and persist for a relatively short time. Howell and Ely found that the

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young of immune rabbits as a rule have antibodies in their serum in appreciable but decreasing amounts from four to six weeks. They state that complement-fixing antibodies are less readily transmitted to the young than other immune bodies.

In human beings, the subject has had little detailed study, although observations indicate that such transmission is practically certain in some instances. The well-known immunity of infants under 6 months to the acute eruptive fevers—scarlatina, measles and rubella—is apparently an evidence of a passive immunity. In diphtheria also, the large proportion of young infants in whom the natural antitoxin can be shown by the Schick test indicates a similar transferred immunity of the antitoxin variety.

The observations recorded by the author illustrate the transmission from mother to infant of the complement-fixing antibodies found in tuberculosis and their relatively transient duration in the infant's blood. The material was obtained from maternity hospitals and out-patient obstetrical cases, the blood from the umbilical cord being studied in 427 cases. A whole bacterial emulsion antigen and inactivated serum were used in making the complement-fixation test. The summarized results gave the following conclusions:

Complement-fixing antibodies present in the mother's serum may be transmitted to her offspring and may persist in the infant's blood for a certain number of weeks. In most instances they have disappeared by the end of the second month and always by the end of the third month. When a young infant's blood gives a positive complement-fixation test for tuberculosis, this reaction is not an evidence of tuberculosis infection in the infant, since these fixing substances are not formed during the first year of life. The presence of such fixation is noted only in young infants when transferred from the mother. The transmission of complement-fixing antibodies in tuberculosis is not accompanied by a transmission of substances which render the skin sensitive to tuberculin.

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#### **Of the Nature of the Antigen in the Complement Fixation Test for Bilharziosis.**

*Geraldine Z. L. LeBas, J. Trop. Med. & Hyg., 25:49, London, March 1, 1922.*

In applying the Bordet-Gengou complement-fixation test to the investigation of helminthic infection dried snails' livers (infected with *Schistosoma mansoni*), were extracted with absolute alcohol. The antigen thus formed would bind complement with syphilitic serum but showed no antigenic properties for normal or positive bilharzia serum. An antigen was then prepared from the residue of the previous antigen and extracted with 50% alcohol, the extract being evaporated to dryness and taken up in normal saline solution. This antigen was found to be quite definite for bilharzia. That Fairley in 1919 found the alcoholic antigen more efficient may be due to the greater solubility of the active principle in alcohol diluted with physiologic saline than in physiologic saline alone. Or it may be due to the increase of the number of positives by the presence of some slightly anticomplementary substance such as cholesterin.

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**The Constitution of the Normal Hemolysin of Ox Serum for Guinea-Pig Blood, with Special Reference to Filtration Experiments and to Conglutination.**

*N. Yoshinare, J. Path. & Bacteriol., 25: 153, Edinburgh, April, 1922.*

The peculiarities of the action of ox serum for guinea-pig corpuscles are found to depend on (*a*) the liability of the antibody, (*b*) its feeble affinity for the corpuscles, and (*c*) the interfering action of certain substances in the serum, these last being capable of being removed by filtration. The early fractions of ox serum passed through a Berkefeld filter may contain antibody but not complement, so are not lytic; such filtrates may however sensitize guinea-pig red cells, but lose this power if heated to 53°C. for thirty minutes. The addition of fresh guinea-pig serum in sublytic doses does not increase the sensitizing power of the latter. No evidence has been found to show that the phenomena in question is due to the direct union of complement and antibody.

Conglutinin is not essential for the lysis of guinea-pig corpuscles by complement and the natural antibody contained in ox serum. Experimental work has shown that filtration removes or alters interfering constituents in the ox serum and renders it capable of sensitizing the red cells of the guinea-pig. Conglutination appears to depend on some distinctive property of ox serum acting together with antibody and complement. Thus portions of filtrate of fresh ox serum not lytic by themselves will cause agglutination which power is lost after treatment with a suspension of staphylococci or after heating to 45-48°C. for thirty minutes. The action is restored however by adding minute portions of fresh guinea-pig serum.

The lytic antibody is fairly stable, but the agglutinating properties deteriorate rapidly on standing at either room or ice-box temperature. The deterioration of these bodies cannot be ascribed to slight changes in the hydrogen-ion concentration of the serum due to contact with the filter.

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**Intravital Hemolysis. II. The Course of Intravital Hemolysis Following Pancreatectomy.**

*R. Bieling and S. Isaac, Ztschr. f. d. ges. exper. Med., 26: 251, Berlin, March 6, 1922.*

The authors first showed that hemolytic serum, injected into pancreatectomized mice and guinea-pigs, produces icterus and hemoglobinuria just as in normal animals. No difference is shown regarding either time or minimum dose. Therefore, the supply of complement must have been furnished by another organ capable of replacing the spleen. The liver was considered in this connection. Of the organs of the hemolytic animals the one in which hemolysis took place shows strong red coloration of the decanted liquid upon trituration after death. Only the spleen decantation was red in intact animals, while pancreatectomized animals treated with hemolytic serum never showed any signs of stronger hemolysis in other organs (liver or kidney). But,

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as icterus and hemoglobinuria set in promptly it must be assumed that the tissue inducing hemolysis is to be found in the whole body and that it is probably identical with the reticulo-endothelial apparatus.

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**The Measurement of the Hemolysin Titer. A New Method.**

*Y. Fukuhara, Ztschr. f. Immunitätsf. u. exper. Ther., 34: 136, Jena, March 21, 1922.*

In hemolytic experiments, in order to have a definite unit for measuring hemolytic capacity, it is necessary to possess as a starting point, a standard complementary serum, whose qualitative and quantitative action does not undergo alteration on aging. The determination of the unit value of the original standard serum was carried out as follows: Total volume 5 c. c. Composition: 1.0 c. c. 5% fresh blood-suspension; 1.0 c.c. of the various amboceptor dilutions; 1.0 c.c. of a 10-fold mixed-complement serum and 0.85% sodium chlorid solution for corresponding supplementation. Sensitization for half an hour at 37° C. Reading after incubation for two hours. The complement was obtained by mixing equal parts of the serum of 3 different guinea-pigs. It was desired to determine that dose which sufficed to dissolve completely 1 c.c. 5% blood suspension. The titer of hemolytic antigenoat blood-serum was determined at 4190 hemolysin units, that of hemolytic antisheep blood-serum at 5320 hemolysin units, in 1 gm. dried serum.

The new method of titrating the serum to be examined consists in employing 2 parallel test series, one of standard serum and the other of the hemolysin serum to be tested. The standard serum is enclosed in Ehrlich's vacuum tubes. For the dilution of the serum, a mixture of two-thirds glycerin and one-third 0.85% sodium chlorid solution is employed. A new solution is prepared every three or four weeks. Each of the tubes of the standard series receives a hemolysin unit of standard serum and each tube of the other series 1 c.c. of prepared dilutions of the serum to be tested. This latter is diluted with physiologic sodium chlorid solution in the proportions 1:100, 1:1000, up to at most 1:1,000,000. By means of these parallel experiments it is found in which serum dilution series the results agree with those in the standard series. For instance, if this is the case in the dilution 1:1000, the serum is said to contain 1000 hemolysin units in 1 c.c. In the experiments it is a matter of indifference whether the complementary serum is derived from one animal or from several, whether it is fresh or has been kept previously for some days. The same applies also to blood-corpuscles. In the application of the Wassermann reaction this method of evaluation will have to be taken into consideration.

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**Experimental Demonstration of the Capacity for Forming Specific Precipitins in Young Individuals.**

*Frant. Luska, Časop. lék. česk., 61: 259, Prague, March 25, 1922.*

In biologic study the colloidal condition of the cell plasma and tissues must always be taken into consideration. The author studied the  
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formation of precipitins in young rabbits after subcutaneous injections of normal horse serum. The degree of flocculability of albumin was determined by alcohol and the concentration of hydrogen in the blood serum. The experiments show that as the concentration of hydrogen ions decreases, the alkalescence of the serum increases. Flocculation of albumin becomes increasingly easy with increasing age. At first Uhlenhut's test was negative; specific precipitins were demonstrated for the first time a week after the second injection, and later the precipitin titer rose uniformly. The parallelism of these 3 processes is quite clear. In comparison with the results in control animals, it was found that the increase in alkalinity commonly observed in young individuals, and the parallel decrease in the stability of the colloids of the blood serum, were a necessary condition for the demonstration of specific precipitins.

The formation of a specific precipitin by an antigen *in vitro* is absolutely dependent on the flocculability of the colloid of the anti-serum. Therefore, when specific precipitins cannot be demonstrated in young individuals 4 to 5 weeks old, this does not prove that these precipitins are not present, but only that at this age specific precipitation is not brought about in the antiserum by antigen *in vitro* according to the methods thus far in use.

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**The Flocculation of Organic Extracts by Normal Serums and Antiseraums.**

*E. Césari, Ann. de l'Inst. Pasteur., 36: 339, Paris, April, 1922.*

Organic cells and liquids contain various mixtures of antigens. The same antigen may occur in different cells or liquids of the same animal species, and the cells and liquids of different species may contain common antigens. The antigen of Forssman, absent in the ox, pig, rabbit, rat, pigeon and man, resists heat and is soluble in alcohol. The serum of rabbits treated with cells containing this antigen (antigen F) produces flocculi when treated with an alcoholic extract of an organ containing antigen F. Césari has sought to determine whether this reaction may be generally used to indicate antigens soluble in alcohol. The method has been investigated with a view to its application in the detection of fraud in food (meat) products. The tissues examined were those of the horse, ox, pig and sheep. Antiseraums were prepared from the blood, liver and spleen of rabbits.

Flocculation is colloidal, one colloid coagulating another. All lipoids producing flocculi with ox serum possess a common antigen. Those flocculating with pig serum contain another common antigen. With respect to human syphilitic serum, there is no relation between the flocculating capacity of lipoids of the heart and liver, and the degree in which their globulins may be precipitated. Tissues which produce flocculating antiseraum also yield flocculating alcoholic extracts. The antigenic substance present in the equine spleen is not composed solely of lipoids, but lipoids probably contain traces of antigen. Flocculation constitutes a test, requiring delicate manipulations, for indicating an affinity between certain elements of serum and certain groups of lipoids. This affinity is natural, in normal ox and pig serum, acquired, in human syphilitic serum, or induced, in serum of rabbits treated with organic

extracts. In the latter case, the effect may be selective, according to the tissues employed. Seroprecipitation and complement deviation, as practiced by means of antiserums, are impracticable for tests in cooked meats, on account of precipitation of the antigens by heat. The commonest fraud consists of the use of tissues of the horse, in place of those of the ox or pig.

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**The Preparation of Cholesterinized Organic Extract for the Serodiagnosis of Syphilis (Sachs-Georgi Reaction).**

*P. S. F. Vermast, Ztschr. f. Immunitätsf. u. exper. Ther., 34:95, Jena, March 21, 1922.*

The difficulties in testing the Meinicke and the Sachs-Georgi reactions consist in the preparation of a good extract with the optimal cholesterin dose. As the obtaining of the exact value of the lipoid-cholesterin mixture in the extract depends largely on the latter's alcohol content, the variable water content of cardiac muscle tissue would exercise an appreciable influence on the cholesterinizability and thereby also on the usefulness of the extract. In order to judge this, the directional coefficient of the aforementioned solubility curve must be known. With this object the solubility table of cholesterin in ethyl alcohol was determined at different temperatures, as well as the cholesterin solubility in mixtures of alcohol and water. Further, the correlation that exists in the extract between the amount of extractive and the cholesterin content required to yield the necessary turbidity for the Sachs-Georgi reaction in the subsequent 6-fold dilution of the cholesterinized extract with physiologic sodium chlorid solution was estimated.

The experiments showed no considerable differences in the proportion of total extractive to protective colloid, but proved that perfectly acting extracts, prepared according to Bok's directions, contain about 3.75 mg. cholesterin and nearly as much extractive.

A quantitatively standardized extract, which, properly prepared, should contain per cubic centimeter as many milligrams of extractive as of cholesterin, was effected as follows: One-half a bovine heart was freed from blood-vessels, fat, sinews, papillary muscles, endocardium and pericardium, and finely ground in a meat grinder; 500 c.c. alcohol (996%) was poured over 100 gm. of the same, the mixture placed in a closed glass-stoppered bottle and shaken about 300 times. This shaking was repeated daily for ten days. The mixture was then filtered and the extractive determined. The extract was diluted with 96% alcohol in such a manner that each cubic centimeter of the diluted extract contained 3.5 mg. extractive. The percentage of alcohol may possess the lower limit of 88% in which 3.5 mg. cholesterin may still be dissolved. The extract, following the 6-fold dilution with physiologic sodium chlorid solution, showed the floccules in the Sachs-Georgi reaction as required of a good extract, because it contained 3.5 mg. extractive per cubic centimeter and the same amount of cholesterin. The Sachs-Georgi reaction was carried out in 7 tubes and yielded the following scheme for the determination of the syphilitic index.

The sixth tube was used for the extract control and the seventh tube for the serum control. Each of the first 6 tubes contained 0.25 c.c.

dilute cholesterol extract. Serum 10% in physiologic NaCl solution was distributed as follows: 0.5 c.c. in the first tube; 0.4 c.c. in the second; 0.3 c.c. in the third; 0.2 c.c. in the fourth; 0.1 c.c. in the fifth; and 0.5 c.c. in the seventh. The second to the sixth tubes, inclusive, contained physiologic NaCl solution 0.1, 0.2, 0.3, 0.4, and 0.5 c.c. respectively. The seventh tube contained 0.25 c.c. alcohol 5% in physiologic salt solution. The index value for the first tube was 0.2; for the second, 0.4; for the third, 0.6; for the fourth, 0.8; for the fifth, 1.0. The tubes were kept two hours at 37° C. and a further two hours at 24° C. in thermostats. The quantitative Sachs-Georgi reaction carried out in this manner agreed very well as regards index value with the Wassermann likewise carried out arithmetically.

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#### Biological Study of the Flocculation Reaction of Sachs-Georgi in Syphilis.

*S. Nicolau and A. Banciu, Ann. de dermat. et syph., 3:97, Paris, March, 1922.*

The new methods of precipitation diagnosis permit further penetration into the secrets of biologic processes governing the reactions concerned. The flocculation which is produced in the reaction of Sachs-Georgi is the expression of the physicochemical conflict between the colloids of the syphilitic serum and those of the cholesterolized extract, the first determining the agglutination and the precipitation of the lipoid granules of the extract. The Sachs-Georgi and the Wassermann reaction are really equivalent in nature, that is, they are phenomena produced at the expense of the same elements. The difference in their optical expression consists in the intervention in the Wassermann reaction of the complement, which, interposed among the element present, protects the colloids of the extract against the agglutinating action of the serum, and thus prevents flocculation.

The flakes are developed exclusively, or almost so, at the expense of the lipoids of the extract, as is shown by their almost complete solubility in ether. Biologically they manifest only the properties of the extract. Neither the flakes nor their ethereal or alcoholic extracts are capable of exercising a single definite anticomplementary action until the addition of syphilitic serum. The antibody of the syphilitic serum, including a part of the lipoids of the extract as well, still remain free, after flocculation in the suspension liquid. This, carefully centrifugalized and decanted to be completely rid of flakes, shows the most distinct anticomplementary properties, even when employed in small doses.

The phenomenon of flocculation, if it modifies the colloidal equilibrium of the substances at whose expense it develops, does not remove their primordial properties: the flakes, which derive some elements from the extract, continue to play their antigenic rôle if they are in the presence of the antibody. The mixture thus acquires anticomplementary properties. The antibody possesses also the faculty of causing flocculation in series of new doses of the extract, as if its properties used only very little in the biologic act that it determines. This phenomenon has led to the comparison of the action of the antibody to that

of the diastases, and to class the phenomenon taking place between the elements of the syphilitic serum and the lipoids of the extract, as a diastatic action, whose final result is the precipitation of the colloids from the extract.

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**The Physicochemical Behavior of the Blood after Intravenous Injections, Especially of Protein with Reference to Anaphylaxis.**

*Hans Rosenberg and Lucie Adelsberger, Ztschr. f. Immunitätsf. u. exper. Ther., 34:26, Jena, March 21, 1922.*

The electric irritability of the vagus and depressor nerves (tested by the blood pressure curve) and of the sympathetic nerve (tested on the rabbit's iris) is altered in the normal animal by intravenous injection of milk, and these injections are capable of producing a protective action against many specific drugs. In healthy human beings or in those not affected by wasting or highly febrile disorders, when fasting and at rest, the precipitability of the fibrinogen fraction of the citrated blood plasma by alcohol and sodium chlorid remains constant for at least one hour. Experiments were conducted by taking from a vein of the arm, after the briefest possible obstruction, by means of a syringe with 0.2 or 0.5 c.c. of 4% sodium citrate solution, this process being repeated after half an hour and one hour. In the individual blood samples the red corpuscles were allowed to subside, the plasma pipetted and treated with the precipitant. It was shown that, following intravenous injection, plasma precipitability with 2 c.c. distilled water was not altered, and with doses of 10 c.c. almost unaltered. With 10 c.c. sodium chlorid solution it was generally slightly diminished transiently; with 0.5% trypaflavine solution (10-12 c.c.) it increased considerably after three minutes. With caseosan and ophthalmosan (1-2 c.c.) there was mostly no immediate increase, but later an increase up to one hour after injection, and at times still materially above the initial value two hours after injection. In animals (rabbit) the injection of milk or ophthalmosan into the blood channel is also followed by pronounced increase of precipitability, the same taking place after reinjection before incubation is completed. Reinjection of sensitized animals after completion of incubation (in anaphylactic shock) does not produce increased precipitability. The precipitability of serum globulins by lactic acid is not altered by sodium chlorid with the same intravenous dosage. By trypaflavine it is altered in the same manner as the fibrinogen fraction proportionally to coloration; by caseosan now rapidly and now gradually increased (after caseosan no positive blood Wassermann reaction has been observed within an hour after injection). In the test-tube, under observance of the conditions of concentration obtaining in the living body, the precipitability of plasma by addition of ophthalmosan and caseosan remains unaltered while it is distinctly increased on addition of trypaflavine and of serum globulins.

It was found that the surface tension of citrated plasma is materially reduced in vitro. In vivo it likewise falls initially after injection but usually increases gradually later. Trypaflavine and sodium chlorid (10%) are without action in the living. The rapidity of sedimentation of the erythrocytes is immediately accelerated by an intravenous injection of caseosan and then remains constant, or may diminish

In vitro caseosan produces increased suspension stability. In vivo 10% sodium chlorid solution leads to retarded sedimentation which increases gradually during the first hour. Trypaflavine has no action. Surface tension, rapidity of subsidence and, after the first hour, plasma precipitability show a certain though not strict parallelism after caseosan injection in the sense of correlated reduction of surface tension, acceleration of subsidence and increase of precipitability. The increased precipitability by trypaflavine in vitro and in vivo is referred to the production of a micellar combination of the dye with plasma albumins or serum albumins and the pharmacologic action of trypaflavine in intravenous application in man is assumed to be the non-specific effect of this complex originating in the organism and embracing proteins in a "foreign state." From the varying action of caseosan on the rapidity of erythrocyte subsidence in vivo and in vitro, it follows that, within a few minutes, extensive changes take place in the organism, which are to be regarded as sequels to the physicochemic reconstruction that also takes place in vitro. The cellular structures may succumb more or less passively to the altered conditions, or they may meet them actively, according to their resistance. Whether the brief transient increase in precipitability results from such processes or from gradual enlargement of particles is undecided. The subsequent permanent increase of the fibrinogen level induces a more persistent tissue reaction. The coincidence of the physicochemic factors as well as the biologic significance of increased precipitability is not yet clear. Generalization on the basis of experiences with caseosan is not yet possible.

The absence of increased precipitability, or of the loss of fibrinogen, in the reinjection of sensitized animals after incubation, might result from rapid thickening of fibrinogen up to formation of floccules, whereby the reduction—or in consequence of acute thrombocytolysis possibly even increase of flocculent substances in plasma and the non-coagulability of the blood would be brought about. The process involved in anaphylactic shock would therefore be equivalent to a precipitous course of the anaphylactoid manifestations following the first injection as regards rate, intensity and extensity.

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**The Intracutaneous Reaction of Nonspecific Substances.**

*Walter Arnold, Ztschr. f. d. ges. exper. Med., 26: 312, Berlin,  
March 6, 1922.*

The following nonspecific substances were examined in regard to efficacy as compared to tuberculin: hypertonic and hypotonic sodium chlorid solutions, carbolic acid (1-2%), and carbolic acid mixed with alcohol (4:1). In the majority of cases the reaction amounts to 5-7 mm. in diameter. With a very strong reaction a very strong positive Pirquet reaction is also observed in most children, due to a strong reacting capacity rather than to the presence of numerous antibodies. All factors that weaken the Pirquet reaction, such as fever, cachexia and pigmentation, also diminish the nonspecific cutaneous reaction. Fever reduces the reaction in infectious diseases and also after vaccination. The Wassermann likewise diminishes the reaction. Pigmentations

weaken the reaction whether natural pigmentations, pigmented nevi or artificial pigmentations produced by radiation are involved. When hyperemia of the skin was induced by mercury vapor radiations or injection of croton oil and olive oil, successful vaccination was much stronger at the untreated control sites. In the infant edemas or light preedemas weaken the reaction, probably because the injected solution is diluted by the edematous fluid. Roentgen rays weaken the reaction if radiation produced hyperemia simultaneously, though the latter only appears after ten to twenty-four hours and whether the children received three-quarter or half erythema doses. At a distance of 6 mm. from the radiation zone the reaction was again normal. Cases occur, however, that react more strongly after roentgenization. In these no alteration was produced by the Roentgen rays. Anesthesia with 10% anesthesin ointment does not alter the reaction in comparison to the control, even when a painless zone is maintained at the site of vaccination.

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#### Anaphylaxis and Hypersensitivity to Poison.

*R. Otto, Ztschr. f. Hyg. u. Infektionskr., 95:378, Berlin, April 5, 1922.*

It is certain that hypersensitivity to serum in guinea-pigs can be transmitted from mother to young, through the passage of the reaction body by placental pathways. To prove a germinal transmission from father to offspring, Otto made studies on young mice whose fathers had been immunized by careful feeding against ricin and abrin, with a view to their reaction against these substances. Of 14 young mice, 5 showed distinct, and 3 questionable, hypersensitivity to the poison with which the father had been treated. Immunity was found in none. Of 7 young mice which were born of immunized mothers only 3 were immune, and these were born soon after the termination of the treatment of the mother. Of the other 4 which were born a longer time after the termination of the treatment, or in which the test was made after the disappearance from their blood of the antitoxin which the mother had transmitted to them, 3 were frankly hypersensitive to the poison.

Accordingly, it is conceivable that a histogenic hypersensitivity is inherited under certain conditions from the father as well as from the mother, but in the latter case, it first makes its appearance when the toxin content of the blood in the young, passively acquired from the mother, has disappeared. Also in true bacterial toxins (tetanus), there is found a sensibility to poison of this kind in the young of previously treated parents; so that eventually even in man a hypersensitivity to certain infectious diseases could be transmitted from parents to their offspring. Whether, in the inheritance of hypersensitivity to poison, we are concerned with the first example of the transmission of an acquired characteristic is not certain. It is possible that the presence of toxin in the sperm might act directly on the germ-plasm, or that in other cases there might be concerned a direct intra-uterine influence exerted by the immunizing agent.

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**The Anatomic Basis of the Anaphylactic Syndrome.**

*T. Silvestri, Policlinico (Pract. Sect.), 29:319, Rome, March, 1922.*

Anaphylaxis is now considered as a defense reaction of the organism, disproportionate to the stimulus, to heterogeneous albumins in the circulation. The phenomenon of this reaction is conditioned on a precipitation of colloids, i.e., by a physico-electric action. The organism does not attack the foreign substances which enter the circulation by means of the antibodies, but defends itself instantaneously either by eliminating them through the emunctories or by precipitating them. According to certain investigators, these humoral reactions are associated, for special reasons, with cellular reactions in some of the tissues, which aggravate the anaphylactic phenomena. While the anaphylactic reaction is often attributed to the precipitation of colloids previously incorporated by the plasma, following the action of the cells stimulated by the antigen which had been changed and absorbed by them in their living colloids, others think that the liberating antigen acts by simple contact, changing the sign of the electric charge of the globulins; their transformation from electronegative to electropositive would result in the precipitation of the colloidal tagmas. The author champions the identity of the anaphylactic shock, protein shock, and toxin infections in general, except that in the latter case the intensity of the reaction is the result of intoxication, while in the former the reaction is entirely out of proportion to the cause and such as to endanger the existence of the organism itself. Since a reaction so intense naturally results in the immediate destruction of the harmful substance, in the majority of cases the violent syndrome rapidly disappears. To explain this reaction, Silvestri has formulated the following hypothesis: the tissues which usually present disturbances of anaphylaxis (bulb, skin, nasal mucosa, and upper respiratory mucosa) are old but fundamental tissues; it is therefore easy to understand that these tissues would lose the physiologic, phylogenetic, and ontogenetic heritage and return to atavistic modes of reaction. Anaphylaxis is thus regarded as a phenomenon of reversion.

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**Anaphylaxis in Isolated Organs of the Frog.**

*M. Kochmann and P. Schmidt, Ztschr. f. Hyg. u. Infektionskr., 95:245, Berlin, Feb. 10, 1922.*

Winter and summer frogs were given intraperitoneal injections of 0.1 c.c. human serum; four weeks later a Läwen-Trendelenburg preparation was made, and the abdominal aorta irrigated with Ringer's solution to which 0.01-0.5 c.c. human serum had been added. The number of drops which escaped from the veins indicated the contraction of the aorta, in all cases. The same results were obtained with bacterial anaphylatoxin and immune serum anaphylatoxin. The controls, which had received no preliminary treatment with human serum, also constantly presented a contraction of the aorta when serum was administered. Preliminary treatment with plasma did not alter the results.

Individual organs were examined for the presence of anaphylactic receptors. Neither the frog heart (when a sufficient quantity of dioxygen was present) nor the intestines, nerves, nervous musculature, nor muscle alone, were injured or influenced by anaphylatoxic serum or by bacterial anaphylatoxin. The authors conclude from these experiments that no sessile receptors or liberated toxins are present in anaphylatoxic serum.

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**Electrocardiographic Examination in the Anaphylactic Shock of Guinea-Pigs.**

*H. Koenigsfeld und E. Oppenheimer, Klin. Wchnschr., 1:849, Berlin, April 22, 1922.*

No cardiac disturbances could be detected electrographically with slight anaphylactic symptoms, such as spasms and respiratory disturbances, but in severe symptoms of shock, condition disturbances were observed which produced absolute auriculoventricular dissociation, the frequency of the auricle being greater than the ventricle. The pulse frequency at first decreased rapidly, then more slowly, until death. These manifestations are not characteristic of anaphylaxis, but are also found in asphyxia caused by exclusion of air. The cardiac disturbances in anaphylaxis in the guinea-pig may be considered as secondary results of asphyxia.

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**The Influence of the Hepatic Vessels on Water Economy and the Hemoclastic Crisis.**

*Gerty Cori and Hans Mautner, Ztschr. f. d. ges. exper. Med., 26:301, Berlin, March 6, 1922.*

Widal ascribed the occurrence of the hemoclastic crisis to flooding of the blood channel by albumin decomposition products although the hepatic veins possess powerful annular musculature, capable of obstructing them. This process is of importance in the entry of considerable amounts of water into the blood channel because fluid is retained in the liver, as has already been observed by Cohnheim and Leichtheim. Hence, spasm of the hepatic veins would represent a regulator of water economy. It seemed reasonable to explain, in this way, the hemoclastic crisis following the drinking of milk. The authors injected 10 c.c. physiologic sodium chlorid solution intravenously into healthy and diseased children and observed leukocytosis in the healthy and leukopenia in the icteric. In the course of further experiments the individuals drank 150-500 c.c. water or Mühlbrunn (mineral water). In the icteric, leukopenia is produced which is replaced by leukocytosis at the end of one hour. In several healthy children leukocytosis persisted one hour. The majority showed leukocytosis that appeared to be interrupted by a remission after twenty minutes. The authors conceive that leukocytes are kept back by the venous spasm whereupon the hematopoietic system throws out leukocytes into the blood channel. On completion of the venous spasm leukocytosis sets in which is terminated through the agency of leukocytolysins. Therefore the compensatory leukocytosis following spasm of hepatic veins in the case of the healthy

liver must depend on intact liver-function. This capacity of the liver for inducing leukocytosis is analogous to its influence on blood coagulation. In infants, leukocyte counts are unreliable, as screaming also produces leukocytosis.

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**Precipitins and the Etiology of Serum Sickness.**

*Stanley Wyard, J. Path. & Bacteriol., 25:191, Edinburgh, April, 1922.*

Practically everyone has assumed that serum sickness and anaphylaxis are the same and the many theories agree in postulating the presence in the patient's blood of antibodies to the serum injected. Wyard undertook an investigation with the object of determining if such was the case. He used precipitins alone, employing the technic of Longcope and Rackmann. Observations were made on 51 men who had received a previous injection or injections of horse serum. These cases were examined 76 times and precipitins were found in 25 of these 39 times and was absent from the others on 37 occasions. No connection was established between serum sickness and circulating precipitin in the patient, a conclusion further borne out by the fact that men whose blood contains these antibodies are in no way more likely to suffer from serum disease than those whose blood is destitute of them. A number of cases were observed from this point of view and not one showed any symptom attributable to serum disease. It thus appears that although serum disease is sometimes accompanied by the presence of precipitins in the blood of the patient, the disease has no demonstrable relation with it. In a table Wyard points out the variability of the precipitin reaction with different strains of antigen, obtained from various commercial houses.

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**Serum Disease in Cattle and Horses.**

*F. Gerlach, Ztschr. f. Immunitätsf. u. exper. Ther., 34:75, Jena, March 21, 1922.*

On the occasion of the application of protective inoculations of cattle against anthrax an anallergic anthrax-immune serum derived not as hitherto from the horse, but from another animal species, had to be employed in order to prevent the occurrence of anaphylactic symptoms in the animals already inoculated with horse serum. One animal, following subcutaneous injections of 5 c.c. each of horse-anthrax-immune serum, which were repeated at longer intervals, reacted 5 times with severe anaphylactic symptoms in which only minimal fluctuations of body temperature were observed. After these serum injections, the animal was refractory toward reinjection each time for about three months.

It was not possible to transmit this hypersensitiveness of cattle toward horse-anthrax serum passively to guinea-pigs and rabbits. The anaphylactic symptoms appearing directly after inoculation in some cattle, protectively inoculated simultaneously with horse-immune serum and culture against anthrax, are not a result of the anthrax culture

injection nor does the injection of anthrax bacilli predispose to their production. Several cattle, which had been previously inoculated with horse-anthrax serum in an emergency, reacted with anaphylactic symptoms when subjected for the first time to serum inoculation. One of these animals died within a few minutes during the course of the serum reaction. The condition showed strong distention; the eyelids were closed from swelling; the tongue was discolored bluish red and protruded from the mouth which was filled with froth and saliva; urticaria appeared over the whole body; the anus and vagina showed edematous swelling, and there was general cyanosis. The postmortem results were as follows: Yellow gelatinous infiltrations in the subcutaneous connective tissue at the edematous parts or those showing pomphili. The lung was remarkably enlarged, light-colored, emphysematous showing numerous small hemorrhages below the pulmonary pleura. The other organs were normal. These postmortem findings were thus typical for anaphylaxis. Such serum reactions in inoculated animals are no longer observed since cattle-anthrax-immune serum is employed for protective anthrax inoculation of cattle.

The experiments were also carried out in the inverse order, horses being injected with cattle serum. Anaphylaxis occurred in 33%, the disease symptoms setting in after a few hours and lasting several hours more. Cattle serum therefore does not produce as severe affections in horses as horse serum in cattle. Serums that have been kept from two months to one year possess the same toxic action as fresh ones. Larger serum doses had no influence on the nature and degree of the serum reaction. Anaphylactic symptoms could be produced in horses by inoculation with 5 c.c. each of human serum or rabbit serum but not with normal pig serum. After a serum reaction the horses were also insensitive toward repeated injections of the same heterologous serum during a considerable period, but this period was not so long as in cattle. The renewed sensitiveness toward the heterologous serum appearing after such a stage of insensitiveness was at first slight but increased subsequently. The insensitiveness toward foreign serums is strictly specific, as during the time in which an animal behaves refractorily toward reinjections of the same foreign serum, another foreign serum is capable of inducing hypersensitive reactions in the same animal. Intravenous and subcutaneous injections produce the same disease symptoms but these appear much more quickly following intravenous injection. Intravenous reinjection of a foreign serum, which took place under conditions from which a severe anaphylactic attack might have been expected, produced precisely the same symptoms of hypersensitiveness as have been observed after first and repeated subcutaneous injections of a foreign serum in cattle and horses. The name serum disease is applied to the reactions occurring after the injection of foreign serum. As a result of the present researches, the greatest caution is recommended in the parenteral administration of foreign albumin species such as is widely employed in veterinary practice in the form of protein therapy. In view of the experiences gained, the necessity exists for employing only cattle-serum for cattle and horse-serum for horses, even in first injections, if the occurrence of serum disease is to be avoided.

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**Histologic Changes in Guinea-Pigs' and Rabbits' Brains in Primary Antiserum Toxicity and in Injections of Toxic Normal Serums. (Carotid—Central Serum Injection).**

*E. Friedberger and P. Schröder, Ztschr. f. d. ges. exper. Med., 26:287, Berlin, March 6, 1922.*

When injected intravenously antisheep blood-rabbit serum kills guinea-pigs. But, as shown by Friedberger and Oshikawa, normal serums and certain animal poisons also destroy rabbits and guinea-pigs when injected into the carotid. The brains of the animals employed were placed entirely in alcohol, embedded in celloidin and small series stained by Nissl's method, and with hematoxylin and Van Gieson's solution. From the guinea-pig experiments it appears that normal serums, as well as immune serums (the latter to a greater degree) cause a toxic action when injected into the carotid. Cattle serum is particularly toxic. One minute after its injection strabismus and rolling movements usually set in. Similar circus and rolling movements were, however, observed in rabbits following carotid injections. The seat of the anatomic changes in the animals with clinical symptoms was the medulla oblongata. In 3 cases several small pale foci were seen macroscopically in the medulla in the Nissl preparation. Microscopically the absence of ganglion cells and accumulations of leukocytes was noted. In 2 other cases there were no such foci, but altered ganglion cells, pyknotic glia and granules. Other cases showed only ganglion cell changes. Vascular changes also play a part, leading to endothelial swelling, leukocyte accumulation and thrombosis. The whole picture is one of necrotic changes. Clinical symptoms are predominant unilateral. The toxicity of the active principle of the antiserum is considerable, as 0.2 c.c. antiserum sufficed to kill a rabbit weighing 1.5 kg. If the water content of the rabbit's blood be taken at 92.6%, there was in 0.2 c.c. of the antiserum 0.0148 gm. solid substance of which protein forms 5.4% = 0.0008 gm. According to Friedberger and Oshikawa, only the albumin fraction is essentially active, and if this be taken at two-thirds of the total protein it appears that 0.00053 gm., i.e., 0.53 mg. of the substance sufficed to produce severe anatomic changes.

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**Note on the Necessity of Checking up the Quality of Sodium Tungstate Used in the System of Blood Analysis.**

*Otto Folin, J. Biol. Chem., 51:419, April, 1922.*

Folin has encountered sodium tungstates which show no alkaline reaction to phenolphthalein, though they are alkaline to litmus. While perfectly pure in the sense that they contain nothing but tungstates, they are unsuitable for blood analyses and will give erroneous figures. One particular variety of sodium tungstates gives perfectly clear blood filtrates but the titrable acidity of the filtrates will be observed to be excessive. Such acid tungstates need not be discarded but can be made serviceable by preparing 100 c.c. of a 10% solution in water, using heat if necessary. After cooling, 10 c.c. of the solution is titrated with N sodium hydroxid to a faint, but permanent, pink reaction, using phenolphthalein as indicator. The pink color should persist for at least

three minutes after the last addition of alkali, since the complex acid tungstates are only gradually and slowly decomposed by the slight excess of alkali added during the titration. In making subsequent 10% solutions of the tungstate the amount of alkali indicated by the titration should be added.

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**A System of Blood Analysis. Supplement III. A New Colorimetric Method for the Determination of the Amino-Acid Nitrogen in Blood.**

*Otto Folin and Hsien Wu, J. Biol. Chem., 51:377, April, 1922.*

This method is based on the very intense and stable color which  $\beta$ -naphthoquinone-sulphonic acid gives with amino-acids. Reagents used: (1) A standard amino-acid solution should contain 0.07 mg. nitrogen per c.c. A stock solution may be made with 0.1 N hydrochloric acid and 0.2% of sodium benzoate. From the stock solution containing 0.1 mg. nitrogen per c.c., the blood standard is made by diluting 70 c.c. with 0.1 N hydrochloric acid to a volume of 100 c.c. Any one of the following amino-acids may be used: glycine, glutamic acid, leucine, phenylalanine, tyrosine and possibly aspartic acid and cystine. (2) Special sodium carbonate solution is prepared as follows: 50 c.c. of approximately saturated solution are diluted to a volume of 500 c.c. The strength of the resulting solution is determined by titrating 20 c.c. 0.1 N hydrochloric acid with the carbonate and with methyl-red as indicator. On the basis of the titration value thus obtained the carbonate solution is diluted so that 8.5 c.c. are equivalent to 20 c.c. 0.1 N acid. The carbonate solution is about 1%. The color reaction between amino-acids and  $\beta$ -naphthoquinone-sulphonic acid takes place very slowly in neutral solutions. The stronger the alkalinity, up to a certain point, the more rapidly the color develops. The correct degree of alkalinity is obtained when 1 c.c. of this sodium carbonate solution is added to 1 c.c. amino-acid solution which at the same time is a 0.1 N solution of hydrochloric acid. The alkalinity is, therefore, represented by a mixture of carbonate and bicarbonate. A drop of phenolphthalein solution should always be used when working with amino-acid solutions of unknown and variable acidity. It is desirable that the alkalinity in the different solutions, the standard and the unknowns, should be approximately the same but not necessarily equal. (3) A fresh 0.5% solution of the sodium salt of  $\beta$ -naphthoquinone-sulphonic acid must be used. For miscellaneous amino-acid determinations when 0.1 mg. nitrogen is the standard, 3 c.c. of this reagent are taken; for 5 c.c. of blood filtrate only 1 c.c. (4) For special acetic acid-acetate solution dilute 100 c.c. of 50% acetic acid with an equal volume of 5% sodium acetate solution. The presence of sodium acetate increases the color of the quinone-amino-acid derivative and retards very much the onset of turbidity due to the liberation of sulphur from the added sodium thiosulphate. (5) A 4% solution of sodium thiosulphate is used to destroy the surplus quinone remaining after the full color obtainable from the amino-acids has developed. It has no effect during the first one or two hours on the colored quinone-amino-acid derivative.

Of the tungstic acid filtrate, 5 c.c. are adequate for the amino-acid determination, but if the filtrate is abundant, 10 c.c. make the process  
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more convenient. Transfer to a test-tube (capacity 30-35 c.c.) 1 c.c. of the standard acid glycine solution (which is the amino-acid solution used by the author as the standard) representing 0.07 mg. nitrogen, and add 3 c.c. water. To another similar test-tube add 5 c.c. blood filtrate. Add 1 drop of 0.25% phenolphthalein solution to each. Add 1 c.c. of the 1% sodium carbonate solution to the standard and then add carefully, drop by drop, the sodium carbonate solution to the blood filtrate until it has approximately the same pink color as the standard. Add another 5 c.c. water to the standard; the volume of the standard is to be twice that of the blood filtrate. Then prepare a fresh 0.5% solution of the sodium salt of  $\beta$ -naphthoquinone-sulphonic acid; add 2 c.c. of this solution to the standard and 1 c.c. to the blood filtrate. Shake to make the solutions uniform and leave them in the dark for from nineteen to thirty hours, at the end of which time add the acetic acid acetate solution, 2 c.c. to the standard and 1 c.c. to the blood filtrate. Add the thiosulphate solution, 2 c.c. to the standard and 1 c.c. to the blood filtrate. Finally add with a blood pipette 14 c.c. water to the standard giving a volume of 30 c.c., and add 7 c.c. water to the blood filtrate (final volume 15 c.c.). Mix and make the color comparison setting the standard at 20 mm. Twenty divided by the colorimetric reading in milligrams, times 7; or 140 divided by the colorimetric reading, gives the amino-acid nitrogen in milligrams per 100 c.c. of blood (5 c.c. of the blood filtrate corresponds to 0.5 c.c. of blood).

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**The Interactions of Oxygen, Acid and Carbon Dioxid in Blood.**

*A. V. Hill, J. Biol. Chem., 51:359, April, 1922.*

The S-shape of the  $O_2$  absorption curve of blood can be explained by the hypothesis that the osmotic pressure of hemoglobin in blood is only  $1/n$  part of the pressure of the  $O_2$  with which it combines, where  $n$  has a value usually of rather less than 2.5. This reduction of the osmotic pressure of hemoglobin is probably analogous to similar effects occurring with weak acids, e. g., boric acid, in the presence of varying concentrations of hydrogen and basic ions, and described under the general heading of hydrolysis. The effects of acid and carbon dioxid upon the  $O_2$  absorption curve of blood can be deduced from the hypothesis that the complex hemoglobin molecules  $(Hb)_n$  and  $(HbO_2)_n$  are like  $H_2CO_3$ , electrolytically dissociated in the forms  $H(Hb)_n \rightleftharpoons H^- + (Hb)'_n$   $H(HbO_2)_n \rightleftharpoons H^- + (HbO_2)'_n$  the degree of dissociation of the latter being far greater than of the former. The same hypothesis accounts quantitatively for the extra carbon dioxid taken up by reduced blood, in excess of that by oxygenated blood. At high carbon dioxid pressures, and at a given  $C_H$ , the taking up of a given volume  $V$  of  $O_2$  results in a diminished carbon dioxid absorption equal to  $V/n$ .

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**An Adaptation of the Folin and Wu Blood Sugar Method Applicable to Small Amounts of Blood. A Comparison of the Blood Sugar Content of Venous and Capillary Blood.**

*Emil J. Baumann and Rae L. Isaacson, J. Lab. & Clin. Med., 7:357, March, 1922.*

Having found the estimation of blood sugar by existing micro-  
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methods unsatisfactory the authors adapted the macrodetermination of Folin and Wu to the estimation of such small amounts of blood sugar as can be obtained by pricking the finger. In this process 0.4 c.c. blood is employed. Ordinary 1 c.c. serologic pipets graduated to the tip in 0.01 c.c. are cut off at about the 0.6 c.c. mark and calibrated to the 0.4 c.c. mark. The pipet is connected with a rubber tube on the end of which a small glass mouthpiece is placed. Blood is taken from the fourth or occasionally from the middle finger of the left hand by pricking with a Hagedorn needle. Gentle pressure is applied if necessary not too near the wound until a large drop of blood collects. This is drawn carefully into the pipet (in the beginning chiefly by capillary), but after about 2 c.c. blood have been obtained very gentle suction must be applied to the glass mouthpiece. The surface of the skin must be kept quite dry with sterile sponges to prevent spreading of the blood. After 0.4 c.c. blood has been obtained it is discharged at once into a 5 c.c. tube graduated in 0.1 c.c. containing 1 c.c. distilled water. The corpuscles settle at the bottom of the tube and a clot will form unless the tube is gently rotated. Frothing must be avoided. The pipet is washed with water several times, the washings added to the tube and the volume brought up to 3.2 c.c. Then 0.4 c.c. of 10% sodium tungstate and an equal volume 0.7 N sulphuric acid are added successively, the tube closed with cork or rubber stopper, shaken vigorously and allowed to stand ten to fifteen minutes. The liquid is then centrifuged at high speed in the same tubes for ten to fifteen minutes, and the supernatant liquid filtered through a very small filter into a 15 or 30 c.c. beaker, after which 2 c.c. of the filtrate is pipeted into a Folin sugar tube and the procedure of Folin and Wu followed exactly as in the macrodetermination. Comparative tables show results obtained macroscopically and microscopically, as well as venous and capillary blood sugar content. It appears that the results of the microdetermination are in close agreement with those obtained by the macromethod of Folin and Wu.

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#### Recent Views on Blood Sugar.

*P. György, Klin. Wchnschr., 1:745, Berlin, April 8, 1922.*

A study of the blood sugar depends greatly on the method of determination. As continued bloodletting greatly increases the sugar content, and taking large amounts of blood is often inadvisable for clinical reasons, not much progress was made until the introduction of Bang's micromethod. While there is still disagreement on many points, it is generally accepted that under normal conditions the blood sugar value is constant at between 0.09 and 0.10%. Two questions arise: Is the blood sugar distributed through both blood cells and plasma? In what form is sugar present in the blood? The first is related to the permeability of the blood-corpuscles. The impermeability of the red blood-cells to glucose in a number of animals has been proved; in man—though it is not uniform—a physiologic permeability to glucose has been demonstrated both in defibrinated blood and in mature blood-cells. Rona and Döblin say that the blood-cells of human beings either contain no sugar though they float in a sugar-containing

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plasma, or the internal sugar content is greater than the external. The author and other investigators tried to determine some laws with regard to the permeability or impermeability of cells by the use of various substances such as acids, alkalis, inorganic salts and various lipid solutions with active surface tension, but failed to obtain uniform results. The second question cannot be definitely answered, though most authors believe that sugar is present in combined form in the blood, this theory being based on the results of filtration and dialysis methods. Bierry determined a glycemic index:  $1 = \text{Free blood sugar} \div \text{combined blood sugar}$ . This index varies in different species but in the individual members it is a constant quantity. A higher value in diabetes indicates a bad prognosis. Rusznyak could not determine any difference in the amount of combined sugar in diabetics and normal individuals by means of ultrafiltration. At least, it is now known that hyperglycemia and not glycosuria is the characteristic symptom of pancreatic diabetes. Continuous observation by the micromethod has led to better knowledge of renal glycosuria; many cases of glycosuria without hyperglycemia have been demonstrated and differentiated from essential diabetes.

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#### A Comparison of Several Clinical Quantitative Blood-Sugar Methods.

*William Thalhimer and Helen Updegraff, J. A. M. A., 78:1383, May 6, 1922.*

This investigation gives 4 quantitative, clinical methods for determining blood-sugar: the original method of Lewis and Benedict, the Myers and Bailey and Benedict modifications of this, and the latest modifications of the method of Folin and Wu. The Lewis-Benedict method was used in only a few determinations, the investigation being confined mainly to the 3 other methods. Results obtained show that the blood-sugar percentages as determined by the Benedict modification are, as a rule, at a higher level than those determined by the Myers and Bailey modification, and the latter higher than those by the method of Folin and Wu. The range of variation, however, in the figures obtained by each method is practically the same. The writer concludes that in interpreting the blood-sugar findings obtained in any laboratory, it is of the utmost importance to the clinician that he be advised of the method employed and also of the range of normal figures for the method as actually determined. The choice of blood-sugar method may be considered a matter of individual preference, provided the foregoing precautions are taken in interpreting the figures obtained. The writers believe that there is some evidence that, in blood containing a high percentage of sugar, the Benedict modification of the method of Lewis and Benedict does not yield results as reliable as the other methods discussed in this article. The Benedict and the Myers and Bailey modifications of the method of Lewis and Benedict, as well as the latest modification of the method of Folin and Wu, have impressed them as being on practically an equal footing in respect to simplicity of technic.

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**Comparative Researches on Blood Sugar Content of the Arterial and Venous Vascular System.**

*Karl Turban, Hoppe-Seyler's Ztschr. f. physiol. Chem., 119:4, Berlin, March 14, 1922.*

Few researches have been carried out on the blood sugar content of the different vascular regions and the statements thereon vary. Experiments were conducted on the dog by simultaneous estimations in arterial and venous blood of the same extremity under the influence of hunger and administration of glucose solution in addition to customary kennel diet. Blood sugar was estimated by Bang's microdetermination. The experiments as summarized in 2 tables show that in the normal feeding as well as in sugar feeding, and with previous fasting days, the arterial blood sugar level generally exceeds the venous. Particularly noticeable was the greater oscillation of the arterial curve after previous fasting days. It would seem that the liver may have lost its capacity for the immediate storage of a larger amount of sugar than of glycogen. This view finds support in the diminished glycogen-deficient liver in accordance with Hofmeister's observations on hunger diabetes, from Bang's experiments on fasting rabbits, and from Barrenscheen's experiments on the artificial glycogen-deficient liver.

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**Free and Bound Water in the Blood.**

*Benjamin S. Neuhausen, J. Biol. Chem., 51:435, April, 1922.*

To explain certain normal as well as pathologic conditions of the body it has been assumed that the body water is partly bound and partly free. From a chemical standpoint the body water could be bound in two ways—by hydration of the ions and by imbibition by proteins. Neuhausen says the great factor in binding water would be imbibition by the colloids. It is well known that lyophil colloids, such as the blood proteins, will imbibe large quantities of water, and that as the quantity imbibed increases the pressure necessary to cause partial desorption becomes less. Highly dispersed particles which present adsorbing surfaces are subject to great compressing forces. A change in the quantity or character of the surface active constituents in the blood would entail a change in the adsorption by the colloids and a consequent change in the compressing force upon them. Since proteins constitute about 8% of blood serum, a marked change in the quantity of water imbibed would be of import and on such a basis a theory of bound and free water could be founded. Various workers have found, however, that in the case of the swelling of gelatin in salt solutions the concentration of these salts in the imbibed water and in the solution is practically equal. Should this be the case with the body proteins, the quantity of water imbibed would have no effect on the colligative properties of blood serum; as a consequence bound or free water could not be detected by the use of these properties. Burgarszky and Tangl determined the freezing point lowering of dog's serum and found values between —0.550 to —0.639, corresponding to concentrations of 0.297 to 0.354 molar. An average of 55 determinations by different investi-

gators is given by Hamburger as —0.571, corresponding to 0.308 mols. To note how near these values approached those at 37.5° C., determinations of the lowering of the vapor pressure of blood serum at about 37.5° C., compared to that of pure water at the same temperature, were made by the author. Alveolar air was bubbled through serum, and air through pure water, and then in each case through sulphuric acid. For the same volume of air passed through, the difference in the quantity of water absorbed by the sulphuric acid was proportional to the difference in vapor pressure. This value divided by the weight absorbed by the sulphuric acid through which the air from the pure water passed gave the relative lowering in vapor pressure. The fair agreement obtained between the calculated molar concentration from the analyses, from the lowering in freezing point, and from the lowering in vapor pressure, supports the conclusion that water imbibed by proteins, as in the case of gelatin, carries practically the same concentration of salts, so that any theory of bound and free water cannot be confirmed or disproved by any physicochemical method based on colligative properties.

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**Lipemia.**

*Fritz Eichholz, Biochem. Ztschr., 128:310, Berlin, March 7, 1922.*

When peptone, soaps or saponin solution are added to any frothing substance in blood serum, or when a small quantity of milk is added to frothing pigment, the froth is seen to collapse on shaking. The mechanism of this action was studied. It was shown that an emulsion of fats or of cholesterol is capable of despumating lecithin in the same way, though with quantitative differences. The despumating action of milk is referable to its property as a fat emulsion. The cause of despumation can lie only in surface tension and surface viscosity as no chemical action is involved. Plateau has shown that in all froth-forming substances the colloidal particles congregate at the surface and there coalesce to form tough membranes. In serum a physical antagonism exists between albuminoids that congregate at the surface, there to form a connected membrane, and lipoids which displace these albuminoids from the surface and attract them to themselves. The despumating action of milk is an effect of adsorption. Experiments with lipemic blood disclose the paradox that a frothing substance (saponin solution) may be despumated by another frothing substance (lipemia serum). Lipemic acids induce surprising adsorption effects. Living tissue is able to separate alkaloids from their adsorption combinations and lipemic serum, contrary to normal serum, has a stronger action on the hypodynamic heart.

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**Prosthetic Group of the Blood Pigment. Formyl Hydroxyhemins.**

*William Küster and Adolf Gerlach, Hoppe-Seyler's Ztschr. f. physiol. Chem., 119:98, Berlin, March 14, 1922.*

Partos has described the preparation and properties of a new hematin-like crystallized body, but was unable to analyze it owing to  
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lack of material. A method is communicated by which the yield of this body was improved. The blood coagulum, extracted with 92% methyl alcohol containing 3% formic acid, was pressed after filtration of the extract. Partos's bodies consist of a formyl hydroxyhemin, in which the rest of the formic acid is present instead of the chlorin in ordinary hemin. Its insolubility in cold soda solution is explained by the fact that it is a monomethylated hemin. The solution of caustic alkalies then effects saponification and at the same time cleavage of formyl. A special hemin type must be involved as the substance is also insoluble in quinin and pyridin chloroform, something not observed before in any hemin preparation. It is insoluble in all organic solvents and has no conductivity. Monomethylformylhydroxyhemin may therefore be regarded as an internal salt. As the action of the diazo methane does not produce further esterification and the hemin obtained, by reason of the manner of its preparation, must nevertheless belong to the B-type in which the one carboxyl has been removed from the sphere of the iron and rendered esterifiable by diazo methane, the esterified carboxyl in Partos's hemin must occupy this position and the second carboxyl must have combined with the one pentavalent pyrrole nitrogen to form a betain-like combination. Thereby, however, the grouping about the iron is determined in this hemin, and on the basis of the coordination number "6" of iron for this hemin it is found that the formyl rest must also participate and the exceptional position of formic acid finds an explanation.

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The Interaction between Blood Serum and Tissue Extract in the Coagulation of the Blood. I. The Combined Action of Serum and Tissue Extract on Fluorid, Hirudin and Peptone Plasma; the Effect of Heating on the Serum.

*Leo Loeb, Moyer S. Fleisher and Lucius Tuttle, J. Biol. Chem., 51:461, April, 1922.*

The authors have previously reported the combined as well as the separate action of tissue extract and serum on fluorid, hirudin, and peptone plasma of vertebrate blood. They have also demonstrated the loss in power of a mixture of serum and tissue extract on standing and the difference in the behavior of fluorid plasma (and similar plasmas) in which coagulation had been prevented through inactivation of calcium on the one hand, and of hirudin and peptone plasma on the other hand. This paper reports a continuation of these experiments in which was observed the combined action of serum and tissue extract on fluorid plasma; the combined action of serum and tissue extract on hirudin and peptone plasma; the effect of variations in the amount of serum on the activity of the mixture (of tissue extracts); the action of unheated and heated serum on fluorid, hirudin, and peptone plasma and the effect of heating on serum. In summarizing the results, the curve representing the coagulation time of the plasma as a function of the time during which the serum and extract were allowed to stand at room temperature before being added to the plasma, can be explained if it is assumed that 2 processes go hand in hand in the mixture; namely the formation of a substance accelerating the coagulation of the plasma

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and of a substance inhibiting in some way the action of the coagulating substance. The character of this curve varies and depends upon the kind of extract and serum which are combined and on the relation of both serum and extract separately with the plasma. With hirudin or peptone plasma the inhibition exerted by the serum on the extract is very great. While with hirudin and peptone plasma the coagulating effect of serum increases with increasing quantities of serum, with fluorid plasma there may occur some deviations from this rule. With the latter the homologous serum is often more active than the heterologous serum; with hirudin and peptone plasma the heterologous serum is generally more potent. Heating the serum to 56° C. for fifteen or thirty minutes destroys or weakens its coagulation action on hirudin and fluorid plasma and weakens the acceleration of a mixture of serum with tissue extract, if this mixture is added at once to the fluorid plasma, but does not greatly alter the effect of such a mixture added at once to hirudin plasma. It diminishes the loss which such a mixture experiences on standing before being added to the fluorid and peptone plasma.

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The Interaction between Blood Serum and Tissue Extract in the Coagulation of the Blood. II. A Comparison between the Effects of the Stroma of Erythrocytes and of Tissue Extracts, Unheated and Heated, on the Coagulation of the Blood, and on the Mechanism of the Interaction of These Substances with Blood Serum.

*Leo Loeb, Moyer S. Fleisher and Lucius Tuttle, J. Biol. Chem., 51:485, April, 1922.*

These experiments continue those reported in the preceding paper, and were made with tissue extracts. The tissues were found to contain constituents which may combine with a substance in the blood serum and thus lead to the production of a substance inhibiting the coagulation of the blood. The quantity of these substances varies in different kinds of cells. If present at all in erythrocytes, it is only in small quantities. The substances can be separated from the tissue coagulins through graded heating. The specific adaptation of the tissue coagulins remains constant, however much the inhibiting substances in the cells may vary in quantity. Therefore this characteristic is believed to exist in the tissue coagulins proper and not to be dependent on admixtures.

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Action of Antigen on Fibroblasts in Vitro.

*Albert Fischer, J. Exper. Med., 35:661, May, 1, 1922.*

Fischer studied the action of an antigen on the rate of proliferation of fibroblasts, to determine whether one part of a fragment of culture grew at the same rate as the other part when a small amount of foreign protein was added to the medium for a long period of time, and whether a change in their respective rates of growth would occur if the fibroblasts cultivated in homogenic plasma and in the same plasma containing a small amount of heterogenic protein were transferred to  
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a medium containing the latter protein under a high concentration. He found experimentally that a small amount of foreign protein added to the culture medium did not modify the rate of proliferation of fibroblasts, while a large amount of foreign protein added to the culture medium markedly decreased the rate of proliferation of fibroblasts cultivated previously in homogenic medium, although not decreasing the rate of proliferation of fibroblasts cultivated previously in the presence of a small amount of the foreign protein. Fibroblasts *in vitro* responded to the presence of an antigen in the culture medium by becoming immunized against its action.

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**Studies on the Anhemoglobinous Nitrogen Content of Erythrocytes. Nitrogen Metabolism of the Tissues.**

*Rudolf Schoen, Biochem. Ztschr., 128:293, Berlin, March 7, 1922.*

The physiologic function of erythrocytes is to serve as carriers of the hemoglobin, for the oxygen exchange between the external air and the body. Hemoglobin, a combination of a highly differentiated protein (globin) with hematin, is the principal albumin of erythrocytes. Besides globin only a small fraction of nitrogenous substance is present. The authors investigated how far the nitrogen content of erythrocytes (other than the hemoglobin-nitrogen) is subject to fluctuations depending on total nutrition, how it behaves under changing (especially nutritional) conditions, and finally whether general conclusions can be drawn regarding the nitrogen metabolism of the cells. If the volume of the corpuscle, its coloring matter and total nitrogen content be known, the anhemoglobinous nitrogen may be determined by deduction of known nitrogen content of human hemoglobin. By serial experiments it would then be possible to follow the alteration of anhemoglobinous nitrogen in relation to pigment.

The volume of erythrocytes was determined with the hematocrit and the erythrocytes count according to Buerker's directions. Hemoglobin was estimated by Sahli's method, and nitrogen by Bang's micro-Kjeldahl method. First the average values for healthy adults were found, then the influence of the color index and volume on the nitrogen value, further the influence of metabolism and of nitrogen excretion on erythrocyte nitrogen and, finally, the nitrogen content of erythrocytes in infections, especially in tuberculosis. The researches show that erythrocyte nitrogen fluctuates and that this is independent of hemoglobin content and volume, so that the fluctuation is related to the anhemoglobinous nitrogen. Under normal conditions the nitrogen value of erythrocytes is constant within an experimental error of 2.5% and shows no daily fluctuations. In the male the average value, with normal hemoglobin content, is 0.00563 mg., in the female 0.00527 mg., to 1,000,000 erythrocytes. At times the value for 1 c.c. blood is of clinical interest. In old age the value is somewhat lower. Pathologic fluctuations of the anhemoglobinous nitrogen may exceed 5-13%, which is usually considered as the physiologic fluctuation. Nutrition has an influence only so far as prolonged undernutrition lowers the nitrogen

value to a minimum. The upper and lower values are reached quickly, depending on whether anabolism or catabolism occurs. Protein-free diet alone does not diminish the value in ten days, but does cause a diminution within a greater period of time. The values for 1 c.c. blood often show distinctly the protein impoverishment of the organism. Deficient nitrogen excretion in renal insufficiency is not expressed in the nitrogen value of erythrocytes and, in part, low values may be found with high rest-nitrogen content of the serum. In certain infectious diseases there is a displacement in the anhemoglobinous erythrocyte nitrogen content that is not conditioned by fever, and is so uniform as to suggest a specific influence. In tuberculosis, there is a displacement in nitrogen metabolism, (probably similar to that of tissue water exchange) that is manifested by alteration of the anhemoglobinous nitrogen content of erythrocytes; this occurs also after tuberculin injection, and is most severe in exudative forms. From this it appears that the displacement of the anhemoglobinous erythrocyte nitrogen content may be regarded as the expression of tissue changes, and of cellular changes generally.

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#### The Glycogen Content of the Leukocytes.

*J. de Haan, Biochem. Ztschr., 128:124, Berlin, March 7, 1922.*

Glycogen is found in nearly all body cells. At times it is present as stored carbohydrate and sometimes as the result of necrobiotic processes in the cells, as in necrotic epithelial cells and rapidly growing tumors. In exudative cells a so-called iodophilia was observed, which could not be demonstrated in other leukocytes. This indicates that leukocytes are stained brown by iodon only under certain circumstances. In any case it points to an altered leukocyte condition. The attempts to estimate the amount of glycogen from the intensity of the staining showed that the pigmentation of exudative cells occurred in the same way and to the same degree whether the exudate was a few hours or one to two days old and, further, that iodophilia was present when the exudate was obtained with 0.9% sodium chlorid or other starchless solutions. For exact examination chemical analysis by Pflüger's method was carried out. To isolate leukocytes the blood was collected in a mixture of sodium citrate and sodium chlorid. On standing, the erythrocytes subsided rapidly. The supernatant leukocyte suspension was pipetted and washed by centrifugation. In order to obtain emigrated exudative leukocytes 200 c.c. sodium chlorid solution was injected abdominally into an adult rabbit, 0.5% starch being added to the sodium chlorid solution. The following day a part of the injected fluid and leukocytes were removed with a trocar and collected in a citrated sodium chlorid solution to prevent coagulation. The glycogen was inverted and the glucose estimated by Bang's method. From the chemical analyses it may be concluded that the glycogen content and iodophilia behave similarly. Iodophilia of leukocytes is present in exudates only a few hours old and bears no quantitative relation to the carbohydrates. The glycogen content of exudative leukocytes is not affected by carbohydrates in the surrounding medium. In blood, glycogen is present to an amount corresponding very closely to that in exudative leukocytes.

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The leukocyte glycogen is not of the kind that is easily removable from fixed cells. It disappears gradually from lytic leukocytes but in fixed cells it is attacked with difficulty even by diastase. Glycogen is not formed in leukocytes as a result of the emigration but is present in the blood, the glycogen content of which is practically confined to the leukocytes. In vitro glycogen disappears from all liquids undergoing cellular lysis. Additions of sodium nitrate or carbon dioxid, which diminish cytolysis may retard the disappearance of glycogen. The antagonistic action of carbon dioxid to lysis is referable to increased hydrogen-ion concentration.

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**On Leukocytosis Produced by the Injection of India Ink Emulsion.**

*Katsuma Nagawo, Japan Med. World, 2:93, Tokio, April 15, 1922.*

Leukocytosis usually follows the injection of small doses of India ink emulsion into the circulating blood, showing 2 stages: an initial and a secondary leukocytosis. The former is preceded by leukopenia of short duration immediately after the injection; leukocytosis reaches its climax in three hours, returning to normal in twelve to twenty-four hours. The secondary leukocytosis develops several days after the receding leukocyte count, reaching its climax in three or four weeks, returning, with oscillations in the count, to normal after a very long period. With larger doses, the preliminary leukopenia persists for a long time, retarding the development of the initial increase, but the latter lasts longer than with a smaller dosage; in addition, the secondary leukocytosis does not develop but secondary leukopenia occurs instead. With still larger doses, the antecedent leukopenia lasts still longer with little or no increase, showing transition into the secondary depression, thus manifesting a long period of leukopenia.

The initial increase is entirely due to an eosinophilia, but the secondary leukocytosis is due to the increased number of large mononuclear lymphocytes and all the other forms of leukocytes. During this stage, the function of the hematopoietic organs is increased, especially with the smaller dosage, the variations depending upon the size of the dose. The oscillations in the peripheral circulation are the same as in the heart blood. These phenomena are not entirely due to the action of the foreign bodies, but probably to mixed substances other than carbon. The secondary leukocytosis, however, must be due to the action of foreign bodies. The chief cause is perhaps the destruction of the leukocytes during the process of digestion, assimilation and the taking up of accumulation of the injected bodies, with a new supply of leukocytes from the hematopoietic organs immediately and persisting long after the injection. This process of destruction and supply is not proportional, resulting in either leukopenia or leukocytosis.

According to Arneth's formula, after ten minutes an incomplete and after half an hour marked left-sided deviation occurs, reaching its climax in one to three hours, returning to normal gradually. This substantiates the view that the leukocytes in the circulating blood are rapidly consumed and destroyed with marked acceleration of the hematopoietic function of the bone-marrow. Ten minutes after the injec-

tion, the anchoring of leukocytes in the lung, liver and spleen was not very marked. In healthy animals, a large number of leukocytes was always found but the preserved leukocytes of the spleen were always decreased in number several hours after the injection. In the bone-marrow, however, a marked leukocytosis occurred after ten to thirty minutes, gradually decreased, and after three hours the percentage of leukocytes decreased to the minimum and then gradually increased to normal. It was thus shown that the anchoring of the leukocytes in the tissues after the injection is not marked. The changes in the spleen show that the demand of the blood for a new supply of the deficient number of the deposited leukocytes effected the expulsion of the deposited leukocytes in the blood. The leukocytosis in the bone-marrow shows that although all the preserved leukocytes may be instantaneously passed out into the blood, regeneration occurs very rapidly and the new cells are also passed out into the blood, giving rise to the temporary wasting after three hours; according to Arneth's formula, the cells passed out are very young forms.

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#### Serologic Researches on the Structure and Origin of Blood Platelets.

*F. Rosenthal and C. Falkenheim, Arch. f. exper. Path. u. Pharmacol., 92:231, Leipzig, March 10, 1922.*

In the following researches on the structure and origin of blood platelets, the authors have trodden a new path. With the aid of serologic methods they have attempted to gain further insight into the common racial relations of the blood platelets to the other 2 great spheres of the hematopoietic system by a study of the receptor structure of blood platelets. Rabbits received injections of: (1) erythrocytes; (2) leukocytes, and (3) thrombocytes from a human being. With the immune serums so obtained agglutination experiments were carried out on erythrocytes, leukocytes and thrombocytes. The results were as follows: (1) Erythrocyte-immune serum agglutinates erythrocytes entirely, leukocytes less and thrombocytes hardly at all. (2) Leukocyte-immune serum agglutinates leukocytes entirely, thrombocytes less and erythrocytes hardly at all. (3) Thrombocyte-immune serum agglutinates leukocytes and thrombocytes and not erythrocytes. The same results were obtained with the agglutinins. From this it is concluded that hemagglutinins and plaque agglutinins are traceable to different antigenic structural groups of cells.

Further experiments dealt with the objection that the antigenic properties of the serum immune toward leukocytes and thrombocytes are directed against the nucleated component of the cells, and that the nonnucleated erythrocytes are therefore not agglutinated. For this purpose the same series of experiments were repeated with fowl's blood, as it contains nucleated erythrocytes and nonnucleated spindle-cells which are ranked with blood platelets. In these experiments, also the erythrocyte-immune serum did not agglutinate spindle-cells and vice versa. The conclusion is drawn that between erythrocytes on the one

hand and blood platelets (spindle-cells) on the other there exist considerable differences in receptor structure while there is agreement between the system of production of leukocytes and that of blood platelets. Consequently the genesis of blood platelets is leukocytic.

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**Thorn-Apple Form and Hünefeld-Hensen's Figures Are Analogous Changes in Various Blood-Corpuscles.**

*H. Brodersen, Anat. Anz., 55:196, Jena, March 15, 1922.*

While thorn-apple forms and mulberry forms of red corpuscles in man are with great difficulty differentiated from each other as regards shape and origin, the thorn-apple forms, as well as the Hünefeld-Hensen figures are produced by an increase of the concentration of salt in the medium; they do not originate from fresh blood-corpuscles, but from cells transformed into a spheric shape. If the water does not produce the spheric form, neither the thorn-apple form, nor Hünefeld-Hensen's figure can be obtained. The Hünefeld-Hensen figures in frogs' blood correspond to the thorn-apple form in human blood. In both forms the spheric center is smaller the greater the increase in concentration of the fluids containing them. The addition of water can produce from both forms the spheric form, but never the original normal form.

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**An Apparatus for the Measurement of Small Quantities of Fluid.**

*J. W. Trevan, Lancet, 202:786, London, April 22, 1922.*

The apparatus consists of a good 1 c.c. syringe (all-glass "tuberculin" or record) and an engineering micrometer head, clamped in line by brass clamps to a  $\frac{1}{2}$  in. steel rod. The micrometer head is graduated in 0.01 mm. meter; its motion pushes the piston of the syringe, and the fluid to be measured is delivered through a steel (preferably rustless) needle under the surface of the diluent (to avoid drop errors). The knob on the piston is either ground plane or drawn out to a rounded point. The instrument can be calibrated roughly by measuring the distance between the marks on the syringe and calculating the volume corresponding to 0.01 mm. ( $=\frac{1}{50}$  of a turn of the head of the micrometer,) or by weighing mercury delivered. The piston must be thoroughly wet with the fluid to be used before setting up. The usual micrometer found in most laboratories can be used if a copper trough is made and arranged so that the anvil of the micrometer fits into the hollow of the trough, one end of which clips on to the knob of the piston, while the other is closed by a flat plate on which the plunger of the micrometer works. The apparatus was designed to measure 0.02 c.c. diphtheria toxin into capillary tubes for the Schick test, but it can be employed for any titration which involves the making of high dilutions—e. g. the Wassermann or other serologic reactions.

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**1f. PATHOLOGY**

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**Rosa-Josepha Blazek: The Bohemian Twins.**

*Sir John Bland-Sutton, Lancet, 202:772, London, April 15, 1922.*

Rosa and Josepha; 2 well-formed girls, were joined by their sacrum, and were double except for their external genitals and anus. The genital canal, though single, led into 2 separate uteri, and the single urethral orifice led into 2 separate bladders. While in the vicinity of Prague, the twins had some urinary disturbances, and Prof. V. Kukula removed a vesical calculus the size of a large hen's egg by litholapaxy. The stone was in Rosa's bladder. At the operation the uniting bond was carefully examined, and the impossibility of a separation operation became evident. It is well known that conjoined twins differ from each other in temperament, tastes and habits. In the Bohemian twins this was especially exemplified in relation to sexual inclination. Rosa had sexual relations with her manager, conceived and gave birth to a living child. The child was in Rosa's uterus, but Josepha as well as Rosa had milk in her breasts. The child was well formed and survives its parents. The twins died within a few hours of each other. The Siamese twins, Chang and Eng Bunker, lived to be 63. Chang, who had been a hemiplegic for some years before death, had a bronchial attack and was found dead in the early morning. Eng died two hours later. The Hungarian twins Helena-Judith expired at almost the same instant. The exception to this rule is the Orissa twins, Radica-Doodica. They were xiphopagous; Doodica had tuberculous peritonitis, and the uniting band was divided by Doyen. Doodica died seven days later, Radica survives.

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**The Last Illness of the Blazek (Grown-Together) Twins.**

*Benj. H. Breakstone, Amer. Med., 17:221, April, 1922.*

Rosa was taller and thinner and looked younger. Josefa was shorter, heavier and looked older. On walking they had to step sideways, although one could walk backwards while the other walked forwards. The abdomen of Rosa was pendulous, and had the linea-stria as evidence of having borne a child. The 2 bodies tapered toward a common point in a V-shaped manner. Beneath the point of union was another V-shaped separation for the legs. Each one, as she lay in bed, had her respective leg over the other, so that one would be under the impression that the vagina and rectum were both in the middle of that point, but it was found that the feet of one were opposite the feet of the other, and between each one's thighs there was a vaginal orifice. The anal orifice was found directly behind where the thighs of both joined, so that this orifice was in the middle of both twins, and was therefore a common anus. Josepha was found to have a rudimentary vagina, with no hymen, and rudimentary uterus, whereas Rosa, who had the linea-stria, had a lacerated perineum, a normal uterus and a lacerated cervix. The rectum was common to both. The sigmoid of Rosa emptied into the rectum about 7 inches above the anal orifice, whereas in Josepha it emptied about 4 inches above. The connection was mostly of soft parts,

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varying in diameter from 9-15 inches. A bony union could be made out between both ilia as well as a probable union between the ends of both sacra terminating into a common coccyx. Rosa was slightly jaundiced, Josefa more deeply so, with an expression of pain and her hand on her abdomen. The temperature of Rosa was normal, that of Josefa subnormal. The writer made a provisional diagnosis of catarrhal jaundice and cholecystitis, or appendicitis, in Josefa, and an almost cured catarrhal jaundice in Rosa, and ordered them to hospital. The temperature, pulse and respiration of both were about the same. It was possible to tell whose bowels moved by watching the abdomen. Especially when Josefa was much jaundiced, and Rosa was not, Josefa's bowels were slate colored, whereas Rosa's were normal. Josefa was constipated most of the time, whereas Rosa had more or less normal bowel movements. There was no bile in Josefa's urine. Josefa became very ill, her symptoms growing steadily more alarming, and Rosa was more or less normal, so that the writer advised that an attempt be made to separate them. This advice was not accepted. It would not have been a difficult matter, even in health, to separate them, and probably save both. The existing rectum could have been saved for Rosa, and if Josefa had lived, an artificial rectum could have been made, or a colostomy. The cutting through of soft parts and bony tissue would not have been a difficult matter.

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**Double Formation of Single Limbs.**

*Appelrath, Fortschr. a. d. Geb. d. Röntgenstrahlen, 29:57, Hamburg, March 20, 1922.*

The subject possessed a hand with 8 fingers, and in place of the radius there was a second ulna. This double formation is probably an ordinary twin arm, or it may be interpreted as a fissure of the blastemic nucleus of the humeral region.

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**A Human Fetus Exhibiting Iniencephaly and Other Abnormalities.**

*William Ivon Hayes, J. Anat., 56:155, Jan., 1922.*

The unusual features of this full time fetus were: (1) absence of the neck; (2) presence of hydrocephalus; (3) deformity of the vertebral column; (4) unclosed vertebral neural arches; (5) large size and peculiar formation of the foramen magnum (being defined in front by the basi-occipital, laterally by the exoccipitals, to which were united the neural arches of the fused vertebrae, and posteriorly by the supra-occipitals, which were united behind the spinal cord, opposite the fourth lumbar vertebra); (6) the diaphragmatic hernia. Following the classification of Ballantyne, the above points led the author to place the monster in the class, iniencephaly.

Mesial sagittal section showed that the deformity was due to malformation of the cranovertebral axis, which was much shortened and formed practically a straight line from the nasal septum to the sacrum. The viscera were consequently pushed downwards and forwards. Ow-

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ing to the shortness of the back, the lower limbs were attached dorsally, while the arms were attached ventrally and only slightly above them, so that the fingers reached down almost to the feet. The article is accompanied by camera lucida drawings of the fetus from the right side and from the front, as well as a median section showing the left side and a section of the craniovertebral axis from the left side.

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**Communication between the Root of the Tongue and the Pharyngeal Vault in a Human Embryo.**

*L. Bolk, Anat. Anz., 55:193, Jena, March 15, 1922.*

In an embryo measuring 16 mm. from vertex to coccyx, Bolk found a short bandlike communication between the back of the tongue and the upper part of the posterior pharyngeal wall. The communication is merely of epithelial nature and very short. It is the persisting median portion of the pharyngeal membrane, which has become thicker instead of rupturing. Into the middle of that prolongation of the posterior pharyngeal wall projects the upper extremity of the dorsal cord. This abnormal state of the cord has produced the persistency of the pharyngeal membrane.

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**A Case of Thoracopagus.**

*W.. Gorn, Klin. Wchnschr., 1:736, Berlin, April 8, 1922.*

The author was called to a patient in whom labor was not progressing in spite of active pains after rupture of the amnion. External examination indicated twin pregnancy; internal examination showed the os completely obliterated, the fetus movable above the pelvic inlet and in the first oblique position and the cord showing only slight pulsation which stopped later. After version it was found that the double fetus was joined at the thorax. An attempt to bring down the feet of the second fetus was unsuccessful; the first head was then delivered and the first fetus turned around 180°. The abdominal wall of the second fetus showed a defect in which loops of intestine could be palpated. Its feet were brought down and the aftercoming head delivered with forceps. The puerperium was normal and afebrile. Each of the two fetuses was 44 cm. long and both were females. Both were completely developed externally and were joined for 9 cm. along the sternum; below the junction there was a large umbilical hernia. They had a common sternum and only one liver. In the umbilical cord there were 4 arteries and 3 large veins. There was a common pericardium and the heart was evidently formed by the growing together of the 2 hearts. The details will be reported in another article. Each duodenum passed into a small intestine which ended in a blind pouch; the large intestine was tolerably well developed in both fetuses and communicated with a loop of small intestine ending in a blind pouch. The other organs showed no special peculiarities. In the mother's family there was a history of cases of malformations, such as harelip, cleft palate and polydactylia.

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**Formation of the Abdominal Fissure. II. Congenital Abdominal Fissure, Occult Cloaca and Rachischisis in a Sireniform Malformation.**

*Gg. B. Gruber and Emmy Best, Ztschr. f. urol. Chir., 8:203, Berlin, March 6, 1922.*

A badly deformed fetus, 31 cm. long, is described, showing the following features: The right auricle was broad, flat, and not articulated. The skull was normal. The trunk was markedly curved and shortened: the thoracic vertebral column was kyphoscoliotic and the lumbar vertebral column was extremely lordotic. The upper extremities were normal. There was a large abdominal fissure, the upper half of which was taken up by the greatly enlarged liver and the lower half was filled with intestines. The left lower extremity was thick, plump, not shortened and ended in a one-toed club-foot directed posteriorly. The right lower extremity descended vertically from the back and was half as long as the left. The leg was entirely absent and a 4-toed, very small club-foot was attached to the thigh. The abdominal viscera were covered by a hernial sac ruptured in the middle, the gap being as large as the palm of the hand; at its deepest point a short stump of the umbilical cord was visible. There was no anal opening and no external genital organs. Midway between the lower ends of the inguinal folds there was a small closed protrusion of skin. In the lateral regions on each side of the abdomen there was an ovary as large as a millet seed with abdominal tubal ends (fimbrias). The thymus was large and bilobed. The aorta arose from the right ventricle and the pulmonary artery originated in the left ventricle as an obliterated cord. The foramen ovale was patent and the ventricular septum showed a small defect. The lobulated structure of the lung was only indicated, but it was otherwise normal. The cecum and ascending colon lay to the left and below in the abdomen and the small intestine lay to the right and above; both the large and small intestine had a common mesentery. The ascending colon showed a direct transition into the sigmoid flexure, which ended in a blind space (ampulla) in front of the sacrum. The right kidney was as small as the adrenal; there were numerous renal cysts; the ureter was absent. The left kidney and adrenal were still smaller and the ureter, bladder and urethra were absent. Connective tissue strands stretched from the blond ampulla to the ovaries and similar bands stretched from the fimbrias downward. The following remarkable features were noted in connection with the vascular relations: The umbilical vessels coursed medially to the left kidney; the femorals either originated in them or emptied into them; the lower portion of the inferior vena cava was absent. The unusual feature of the skeleton was the presence of only 3 lumbar vertebrae and also the very marked lumbar lordosis; the second lumbar vertebra had a cleft spinous process and in the third the entire right half was absent. The sacrum consisted of 4 fused vertebrae, and the right half of the sacrum and the coccyx were lacking. As a result of the marked torsion of the pelvis and the severe grade of lordosis of the lumbar vertebrae, the anterior surfaces of the ilia were directed downward and the posterior surfaces upward. The symphysis pubis was posterior, the ischia protruded upward, as did also the angles of

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the pubis. The acetabula were directed posteriorly and upward and the right one was atrophied. The right rectus abdominis was almost completely absent, as was also the musculature of the right leg.

The histologic examination revealed as the most important finding the presence of sweat glands, hair clumps and sebaceous glands, which were directed inward, at the terminal blind sac of the intestine; the intestinal wall showed the typical picture of the colon, and in the surroundings circularly arranged cross-striped musculature. It was a question, therefore, of a secondarily constricted, ectodermal anus; there were also small cysts in its vicinity and glands lined with cylindric epithelium; these structures were in connection with the rudiments of the bladder. The intestinal wall, elementary bladder and skin sac formed a labyrinth of connecting passages, which was surrounded by smooth and cross-striped muscle, connective tissue and fatty tissue. Strands, which spread from it laterally, proved to be ureters. The right showed a colossal muscle hypertrophy, and near the bladder the ureter was only a muscular band. The left ureter was fusiformly dilated in its lower third and then obliterated. Glia tissue was found in the lower portion of the sacral defect and a few ganglion cells and adhesion of the spinal cord meninges with the surroundings were demonstrable.

The cause of this malformation lies in a disturbance of the direction of the growth of the body end during the second month. The caudal end of the embryo was strongly bent posteriorly, thereby preventing the union of Müller's ducts and the development of the bladder, and the cloaca persisted. The skin portion directed posteriorly was due to a secondary disturbance of development. The cloacal membrane had ruptured early, but had soon united again as a result of the marked mesodermal development of the vascular soft parts, with invagination of the proximal parts. The hypoplastic cystic kidneys, which are not rare in such cases of sireniform malformations, are due to fetal inhibition of development and further maldevelopment; the same applies to the obliteration of the ureters. The muscular hypertrophy of the ureters should be considered as an excess growth. The labyrinth-like configuration of the bladder is probably due to the constricting growth of the mesoderm. The vertebral defects correspond to anomalies of growth in the primitive vertebrae and influence the development of the abdominal viscera.

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**Deformed Fetal Pelvis.**

*Gg. B. Gruber, Arch. f. Gynäk., 115:615, Berlin, Feb. 16, 1922.*

The pelvis of 4 fetuses with typical disturbances in development are described. (1) Eventration with intestinovesical scissura; reversed pelvis with ischial cavities turned laterally and backward, forward and outward; hip-joints directed backward; femurs rotated outward; os sacrum very lordotic with the upper branches of pubis in the same plane, and with a scoliosis whose convexity is directed toward the right side; large scissura in the vertebral column at the lumbosacral level with myelocystocele. (2) Eventration, which in an amniotic pouch (similar to the sac of a hernia) enclosed an intestinovesical fissure; reversed pelvis with considerable lordosis of the sacrum (opened at the back) without any articulation with the ischia; at the posterior part, adhesion

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between the posterior spines of the ischia; broad fissure of vertebral column; pubic symphysis gaping. (3) Eventration with a cloaca and other deformities of the urogenital system, with a siren-like deformity; closed pelvis, badly developed on one side; considerable lumbar lordosis, severe defects and fissure in sacrum; the left ischium directed outward and backward; the acetabulum looking backward; the thigh in outward rotation; severe atrophy of the right leg. (4) Sirenomelus with pseudosympodia; both extremities united in the soft parts; iliac bones turned outward and backward; the inferior branches of the pubis forming a sole mass with the ischiatic tuberosities; hip-joints approximated to one another in posterior direction; thighs rotated outward; no defect in the sacrum and coccyx.

The common findings in these 4 pelvis are the abnormal direction of development of the lateral parts and the asymmetry. This inequality in development probably depends upon a disturbance of the anlage of the axial skeleton and of the wall of the trunk. As the anlage of the pelvis appears later on and independently of the vertebral column and as the proof of the disturbed direction of growth in the mesodermal blastema must admit a cause influencing extensive regions, the deformity must, then, be assigned to metamerid disturbances of development in the first to the third embryonal week. The siren deformity and the siren pelvis are genetically related to the other misshaped pelvis. The essential feature is a disturbance in the direction of development; in that case, there has been an energy of development limited on one side; the sympodia is a secondary phenomenon.

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**Origin of Relaxatio Diaphragmatica.**

*K. Kuré, T. Hiramatsu, K. Takagi, M. Nakayama and S. Matsui,*  
*Ztschr. f. d. ges. exper. Med., 26:164, Berlin, March 6, 1922.*

Relaxatio diaphragmatica is generally found on the left side. The causes are differences in pressure or slight resistance of the diaphragm. Injury due the phrenic nerve may be of importance. In 1914 Kuré and his associates showed experimentally that extirpation of the celiac ganglion diminishes diaphragmatic tonus. But no picture of true relaxatio diaphragmatica resulted as the operations were conducted on dogs, cats and rabbits, which possess large livers. Therefore the operation was performed on 4 apes. In spite of gastric distention it was not possible to produce relaxatio diaphragmatica. This was successful, however, in 7 apes when evulsion of the left phrenic nerve was carried out in addition to destruction of the celiac ganglion. It was shown on 34 other apes that division of the motor root of the left phrenic nerve immobilizes the left diaphragm. Extirpation of the left cervical sympathetic produces only slight elevation of the diaphragm. Eradication of all sympathetic fibers (they also traverse the splanchnic and phrenic nerves) likewise causes only slight evulsion of the left phrenic nerve frequently excessive, relaxatio diaphragmatica. The latter is always attained by simultaneous evulsion of the phrenic nerve of the left side and extirpation of the left celiac ganglion. Evulsion of the right phrenic nerve and extirpation of the right celiac ganglion is not followed by relaxatio diaphragmatica as it is prevented by the large hepatic lobe.

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The roentgenologically visible depression of the diaphragm deprived of the phrenic nerve is due to thoracic movement and is therefore a passive one during inspiration. Experimentally induced relaxatio diaphragmatica produces degeneration of the diaphragm extending up to the margin of the paralyzed side. This may convert the diaphragm into a connective tissue-like plate if the animal remains alive long.

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**Gastric Glands in the Extroverted Distal End of the Vitelline Duct.**

*G. W. Nicholson, J. Path. & Bacteriol., 25: 201, Edinburgh, April, 1922.*

Nicholson believes that heterotopic tissues do not receive the amount of attention they deserve from the point of view both of development and of tumor formation. The patient, a girl aged five months, was born with a so-called umbilical polypus. There were no other malformations nor did the family history show predisposition to any sort of deformity. The site of the umbilicus was occupied by a raised rounded mass, about 1 cm. in diameter, with red granular surface. Its circumference was rolled and passed abruptly into the skin of the abdomen. At its center was a small round opening, from which a slight amount of mucus and contents of the small intestine escaped. This matter contained digestive ferments but had no fecal odor, so that the communication with the bowel cannot have been low down. It was ligated at the level of the line of union with the skin. Recovery was uneventful. The specimen was cut through the middle when the writer received it. It showed the end of a narrow duct, lined by a distinct mucous membrane, which was evaginated in its distal part to form the umbilical polypus. This case is obviously one of a patent vitelline duct whose distal end was evaginated in the usual manner. The part of the vitelline duct within the abdomen was lined by mucous membrane identical with that of the small intestine. Where it was evaginated on to the surface it possessed a gastric mucosa. The line of union was abrupt and well defined, corresponding to the opening of the duct on to the polypus.

The vitelline duct and its distal end, when this alone persists, are usually lined by mucous membrane of the small intestine. This is invariably so in the greater part of the duct, all the heterotopic structures that have been recorded being found either in its umbilical portion, or at the apex of Meckel's diverticulum. Displacement and heteromorphosis are the 2 possible explanations of the occurrence of gastric glands in the vitelline duct. These give rise to the following questions: Is it possible for cells that were destined to form a part of the mucous membrane of the stomach to be displaced to this spot? If not, can the cells of the duct become differentiated in this direction? Nicholson affirms that to assume that all the parts of the fully developed alimentary canal are already mapped out in the corresponding regions of the entoderm in the earliest days of its formation is to carry the doctrine of preformation to an unwarrantable and absurd conclusion. It is quite impossible for displacement to occur at a later stage of development. However, patches of heterotopic epithelium have been found in many parts of the alimentary canal and its diverticulum.

The findings of Schaffer and Poindecker show that the cells of the endoderm may undergo differentiation in 2 directions, the alternatives being squamous and columnar epithelium, both of which are normally present in the alimentary canal of the adult. The columnar epithelium becomes more fully differentiated into the characteristic mucous membranes of the various segments of the gut. These characters are to a certain extent interchangeable during the ontogeny of the individual. The writer's observations of newly formed pyloric glands in tuberculous granulations of the vermiform appendix seem to indicate that all the cells of the entoderm retain their primitive potentialities throughout their whole lives, and that these can be called out by active proliferation in regenerative processes.

The presence of gastric glands at the distal end of the vitelline duct proves that those cells of the endoderm, which are usually absorbed in the early weeks of development, possess potentialities identical with those of the cells that form the alimentary canal. They can undergo differentiation into glands of the stomach and into squamous epithelium. But it is only at the distal end of persistent remnants of the duct, in umbilical polypi, and at the apex of a Meckel's diverticulum that these heterotopic formations occur. Were they due to a displacement of cells during development, there is no reason why they should not be found in all parts of the duct. Their exclusive presence at the distal end of its remnants indicates that they are formed in its original situation by abnormal differentiation.

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Inflammations in Their Relation to the Nervous System.

*Hermann Groll, Beitr. z. path. Anat., 70:20, Jena, Feb. 14, 1922.*

As it appears to be definitely established that paralysis of the sensory nerves exerts an inhibitory effect upon the initial stage of inflammation, Groll attempted to determine the mechanism of this antiphlogistic effect. To this end, accurate knowledge of the vessel innervation was first required. Suitable tests in the frog showed that arterial hyperemia through dilator peripheral stimuli could be induced by the local application of pilocarpin, physostigmin and probably also a solution of ammonia, and, under certain conditions, by the application of heat.

Local application of veronal, atropin (10%), mustard oil, tuberculin, and probably also veratrin, to the web of a frog's foot produces a neuroparalytic arterial hyperemia due to peripheral paralysis of the constrictor apparatus. Similar results are produced by the application of heat or cold, and by the injection of large amounts of curarin into the lymphatic sac. When 1% atropin is applied to the hyperemic web, contraction of the dilated arteries is produced through paralysis of the nerves of dilatation. All substances, vasodilators or vasoconstrictors (including heat and cold), act directly upon the peripheral vasomotor apparatus of the vessels of the frog's web. When applied locally to the web, irritation of the sensory nerves, a reflex process, is necessary to produce an effect.

The results of these experiments show that at least some of these poisons attack the nervous portion of the peripheral vasomotor apparatus, and that their poisonous effects are specific.

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A series of inflammation tests was made in frogs and warm-blooded animals (guinea-pigs). In the former, section of the sciatic nerve and degeneration of its peripheral branches may produce arterial irritative and neuroparalytic hyperemia. The initial hyperemia in the inflammatory area was neuroparalytic in every test; it is a mistake to assume a reflex arterial irritative hyperemia in the early stages of inflammation. In warm-blooded animals, arterial neuroparalytic hyperemia results in spite of anesthesia, provided the stimulus can reach the vessels and directly influence the vasomotor apparatus. Inflammatory edema (fluid exudate) can appear in the anesthetic area as well as in the region of normal innervation. The amount of exudate depends in part upon the condition of the circulation. The nature of the tissues is still more important (permeability of the vascular wall and alterations of the pressure of tumefaction). The inflammatory cellular infiltration may be the same quantitatively and qualitatively in the anesthetic area as in that with normal nerve supply. All the changes in the course of inflammation that can be observed after section of the nerve are independent of existing anesthesia and are apparently only an indirect result of the nerve section, resulting through the mediation of the circulation and through altered conditions of tissues; they can be evoked by the proper application of suitable drugs.

Clinical experience with changes in the course of an inflammatory process by nervous influence (nerve section in tuberculosis of the larynx, and anesthetics), do not prove that anesthesia is the important factor. Often there is a changed state of the tissue, a diminution of the pressure of tumefaction. It must also be borne in mind that section of a nerve, even when no motor fibers are eliminated, may exert a therapeutic influence by keeping the inflamed area quiet; absence of pain may abolish much reflex motion.

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**Tissue Respiration in the Vasomotor Reaction.**

*H. Gessler, Arch. f. exper. Path. u. Pharmakol., 92:273, Leipsic, March 10, 1922.*

It has been found impossible to draw a sharp dividing line between lighter degrees of inflammation and dermographism. While it is fairly generally agreed that the hyperemic area in dermographism is to be regarded as a central reflex, the views on the origin of the local vasomotor reaction differ considerably.

Gessler has obtained results in the course of researches on tissue activity in inflammation which are closely related to Virchow's view that tissue and capillaries are a functional entity and that consequently the caliber of the capillaries depends on the condition of the tissue. It was shown that tissue substance metabolism is considerably increased in inflammatory foci outside the necrotic zone. Oxygen consumption was measured in excised cutaneous strips (of human beings and pigs) that were under the influence of various pharmaceutic substances and physical agents. The following results were obtained: Heating to 40° C. increases oxygen consumption about 80%; to 48°, about 100%. At 52° oxygen consumption sinks to zero (tissue death). The living human being's skin is stimulated vasomotorially by the fatty acid group, the degree of reaction increasing with the number of hydrocarbon

groups. On the other hand, excised skin shows decreased oxygen consumption if dilute solutions of the fatty acid are employed, as, for instance, 0.03 N. In strong solutions (0.01-0.1 N acetic acid), oxygen consumption is increased up to 100%. This fact is explained by assuming that in the living body the acids act as a result of their lipoid solubility, while in excised skin their action corresponds to their hydrogen-ion concentration. The lipoid-insoluble inorganic acids, e. g., nitric acid, are inactive in the living body, but they also act on excised skin by reason of their association. The conclusion is drawn that inflammatory hyperemias are produced by heating and by chemical stimuli, owing to increased metabolism.

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**Concentration of Albumin and Sodium Chlorid Absorption of the Blood Serum in Edema.**

*Franz Kisch, Klin. Wchnschr., 1:848, Berlin, April 22, 1922.*

Eppinger's hypothesis of the origin of edema postulates that edema results from the increased exosmosis of albumin from the blood through the injured capillary walls into the fluid of the subcutaneous tissue; simultaneously sodium chlorid is retained in the body and this is accompanied by increased accumulation of fluid. The author's studies showed a strikingly low amount of albumin in the serum in nephrosis, abnormally high content in myxedema, and a normal albumin content in cardiac and nephritic edema; the sodium chlorid content of the serum varies greatly in the various edemas; the absorptive capacity of the serum for sodium chlorid (when added in excess) is decreased in all diseases with intense edema, but in myxedema and nephrosclerosis there is a normal value.

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**Degeneration and Regeneration.**

*Paul Ernst, Deutsch. med. Wchnschr., 48:409, Berlin, March 31, 1922.*

Regeneration is assimilation for the purpose of building up new living tissue. It is observed in the restoration of protozoa (up to two-thirds of their body volume if the fragment is still in possession of its nucleus), of polyps and worms. In the lower animals, like develops from like, but where this is not possible nature takes her material where she can find it. This cannot be applied unconditionally, however, to higher animals. Amphibia regenerate better than certain worms. Young animals regenerate better than adult ones; external conditions such as light, heat and the surrounding medium play a certain part in regeneration. Regeneration in man is controlled by the law of specificity of cells and tissues. The exceptions chiefly concern differentiation in embryonic development, loss of differentiation and metaplasia.

Regenerative capacity decreases with increased differentiation of the cell, therefore excretory ducts regenerate better than fully developed glands, epithelial and connective tissue cells better than nerve and muscle cells, and the connective tissue structure of the blood vessels better yet. In the healing of wounds young connective tissue serves for regeneration. There is mitosis of connective tissue cells, and transformation of

fibroblasts into collagenic and elastic fibers. In the structure of scar tissue, blood-vessels are utilized which originate from mitotically divided capillary endothelium and it is possible that from their walls cells are split off which act as formers for young connective tissue. For the protection of the cicatricial new growth, epithelium is utilized, which originates in less differentiated cells (crypts of the intestinal and uterine epithelium, excretory ducts of the sebaceous and sweat glands, and the like). Bone and cartilage develop in regeneration from the perichondrium and periosteum. Bone is such a highly developed tissue that it is not capable of regeneration. The new growth of smooth muscle fibers is slight. Striped muscle fibers increase by hypertrophy rather than numerically. Neuroglia has a considerable capacity for regeneration. New growth of ganglia has never been definitely demonstrated. Regeneration of peripheral nerves is possible. Wound healing, pathologic organization and callus formation belong in the domain of regeneration. Metaplasia, transplantation, grafting and parabiosis are related phenomena.

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**Cicatrization of Wounds. XIII. The Temperature Coefficient.**

*Albert H. Ebeling, J. Exper. Med., 35:657, May 1, 1922.*

Cicatrization is a complex phenomenon, involving many factors, alterations of the viscosity of surface tension of the fluids and the anatomic structure playing a rôle as important perhaps as that of chemical transformations. Ebeling's attempts to measure the value of the temperature coefficient of the phenomenon were made to ascertain whether physical or chemical changes are more especially involved. Experiments were done on 2 young alligators. A flap of skin on the ventral surface of the body was resected with a sharp knife and the outline of the wound carefully traced. The animals were then placed in a room at 38° C. until the wounds had healed. Several days later a second resection was made on a different area of the ventral surface, as nearly as possible of the same size and shape as the first, and the animals were then kept in a room at 23° C. In the warmer room the rate of cicatrization was greatly increased, which was to be expected, since wound healing is closely related to the phenomenon of growth and regeneration. Changes in temperature are known to affect metabolism and development of certain organisms in the same manner as a chemical reaction. In spite of the complexity of the factors which bring about the cicatrization of a wound, it appears, therefore, that the velocity of the phenomenon depends on the rate at which certain chemical changes take place.

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**The Reticulo-Endothelial System.**

*Hans Eppinger, Wien. klin. Wchnschr., 35:333, April 13, 1922.*

In place of the earlier physical methods of staining, a vital staining of certain organs is now accomplished by the intravenous or subcutaneous injection. Among the stains so used are pyrrol blue, trypan blue and isanamin blue, which circulate in the blood selecting certain kinds of cells occurring at definite places in the body. Goldmann calls them

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pyrrol cells. In the liver these pyrrol cells are found near the capillaries of the portal vein; it is doubtless a question of staining of Kupfer's stellate cells. Pyrrol blue is also stored in the red pulp of the spleen, which offers an opportunity for elective staining on account of its content of reticular cells. The same thing is true in the lymph glands. The blue which is perceptible microscopically is due to a staining of protoplasm granules in the reticulum cells. A blue staining also takes place in the connective tissue of the skin and in the lungs. There is a relationship between the staining of the liver cells and those of the lungs; when the former are only stained slightly the latter are stained deeply and vice versa. According to Aschoff these same cells are stained red after the injection of lithium carmin, and moreover this reticulo-endothelial complex (Aschoff) shows a capacity for storing collargol and cholesterol.

Aschoff speaks of the possibility of blood cells, which were at first sessile, becoming separated from their original location and migrating. These are the so-called histiocytes, which are similar to large mononuclears and may be of reticulo-endothelial origin. These cells have the capacity for combining and fixing for a long time in their granules, substances that are dissolved in the blood; they take part in important metabolic processes. By this method of analytical staining it has been possible to discover a morphologically related system of cells. This cell complex plays a great part in hemolytic icterus, in which the spleen is enlarged. The erythrocytes are broken down here. With splenectomy the icterus disappears, blood metabolism returns to normal; therefore, the reticulo-endothelial cells of the spleen are closely connected with the catabolism of erythrocytes. In the former iron can be demonstrated and bilirubin is found in the efferent vessels of the spleen. But in hemolytic icterus Kupfer's cells of the liver must be considered as erythrocytes are catabolized here also; the spleen, however, is the most important organ.

In pernicious anemia, where the highest bilirubin values are found in the bile or in the duodenal fluid, there is a condition analogous to that in hemolytic icterus. The poverty of the blood is not due to weakness of the bone-marrow as the functional capacity of the latter is increased. One characteristic of pernicious anemia is an increase in hemolymph glands, which, standing functionally midway between the spleen and lymph glands, have in common with the spleen a capacity for phagocytizing erythrocytes. The behavior of Kupfer's stellate cells is interesting; while in hemolytic icterus they show only a diffuse imbibition with iron, in pernicious anemia they show an intense storing of iron, similar to that which occurs after the injection of iron. Moreover the Kupfer's cells are filled with phagocytized erythrocytes. In pernicious anemia the reticulo-endothelial system is the chief point of interest; its cells are in a condition of hyperfunction, and for this reason splenectomy does not do very much good, for in addition to the spleen Kupfer's stellate cells and the hemolymph glands are active. Hematin, the pigment of the erythrocytes, breaks up, on catabolism, into bilirubin and iron; the bilirubin is waste matter and is excreted, but the body is very sparing in its excretion of iron. Other diseases in which the reticulo-endothelial system is involved are aplastic anemia, polycythemia and cirrhosis of the liver.

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**Plasma Cells and Mast Cells.**

*F. Jiménez De Asúa, Arch. de cardiol. y hematol., 3:92, Madrid, March, 1922.*

The blue-staining plasma cells are normally present in connective tissue and are abundant in chronic inflammations and in the stroma of many tumors. They may possess one or more nuclei, which are usually eccentric and surrounded by a clear halo or by a group of fine spherules. The cells are basophil. Giant cells of large size and containing 2 or 3 nuclei belong to this group. The plasma cells may contain strongly basophil granules, which may be extruded. The latter may agglomerate to form 1 or 2 larger granules, staining black with silver. The protoplasm is sometimes filamentous, or it may consist merely of a narrow ring enclosing the nucleus. Vacuoles may be contained in the cytoplasm. Large spheres sometimes occur, compressing the nucleus or rupturing the cell. Not all strongly basophil cells are of the plasma cell group, which should include only the forms described and a few transitional or degenerate forms. The other basophil, blue-staining cells should be termed pseudoplasma cells. True cyanophil cells are derived from lymphocytes of the connective tissue by transformation. The intermediate cell contains abundant protoplasm and a circular nucleus, and is somewhat more basophil than the original lymphocyte. The types described above represent developmental phases. The plasma cells are secretory. The granules of the mast cells are of all sizes. The fine granules may be basophil and may stain a normal tint, while the large basophil granules may be atypically tinted. The nuclei resemble those of the plasma cells. The mast cells originate from the lymphocytes, but have a nongranular phase, the protoplasm being slightly basophil, while the round nucleus contains peripheral spherules of chromatin. Both types (plasma cells and mast cells) are thus derived from lymphocytes and pass through a phase in which the protoplasm is slightly basophil and the nucleus is spherical. Several beautiful plates are given.

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**Studies on the Adaptation of Albino Mice to an Artificially Produced Tropical Climate. I. Effect of the Various Factors Composing a Tropical Climate on Growth and Fertility of Mice.**

*E. S. Sundstroem, Am. J. Physiol., 60:397, May 1, 1922.*

As a preliminary study on the acclimatization of man to a tropical environment, a number of experiments were carried out on the physiologic behavior of mice in an artificial tropical climate. The principal object was to compare the growth of mice brought into the hot room at an early age (usually 3 weeks) or born in this environment, with the growth of mice continuously kept at ordinary room temperature. In addition to the control series that was reared in subdued light the author kept in the "temperate" room two other series, "immigrants" and "descendants" (referring respectively to mice that were transferred to the new environment when 3 weeks old and mice that were born there) in which the animals were exposed to strong artificial light. In the hot room two corresponding series of "light" mice were kept. The effect  
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of air in motion was studied only in the hot room and in subdued light. The "tropical" room had an air capacity of 6.5 cu. m., and was fitted with double walls, separated by an air space. The heating of the room was accomplished by an electric hot plate. The dry bulb temperature of the hot room was kept about 10° C. above the temperature of the room of the controls. The high humidity of the "tropical" room was maintained by placing a large basin filled with water on the hot plate. The source of the light consisted of "Mazda" globes, two 60 watt lamps being employed in the temperate room and one 100 watt lamp in the hot room. As mouse cages, enameled basins, 11 inches in diameter, were employed, and as a rule 6 animals were confined in each cage. The food was the same for all series, chiefly a mush prepared with yellow corn meal, rice, rolled barley and powdered meat scraps. Greens were supplied once or twice a week and all mice had free access to water. The mice were weighed at weekly intervals for 20 weeks and the weights recorded to the nearest 0.1 gm. The tabulated results show that exposure to artificial light at ordinary room temperature accelerates the growth of mice. Confinement in a stagnant hot and humid atmosphere retarded the growth of mice that were transferred to the new climatic environment immediately after separation from their mothers. Succeeding generations of mice born in a hot and humid environment show a different behavior in their reaction to this environment. The first native generation may develop normally, while the 2 next generations may elicit the greatest effect of the hot climate, at least as far as their growth is concerned. Exposure to artificial light in humid heat added to the retarding effect on growth produced by the latter climatic factor. Circulation of the hot and humid air neutralized partly the unfavorability of the tropical environment for the growth of animals. The growth of the male mice was found to be less retarded by an unfavorable environment and more accelerated by growth stimulating climatic factors than the growth of female mice. The growth of mice that were born in a new environment but the intrauterine development of which fell partly outside this environment, was faster than animals transferred to the same environment when in a growing state. The fertility of a mice colony when normal is not necessarily diminished by confinement of the mouse in humid heat for several generations.

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**Studies on the Adaptation of Albino Mice to an Artificially Produced Tropical Climate. II. Relations of the Body Form and Especially the Surface Area to the Reactions Released by and the Resistance to a Tropical Climate.**

*E. S. Sundstrom, Am. J. Physiol., 60:416, May 1, 1922.*

Experiments to determine whether the surface to weight ratio undergoes any change in heat, when animals of the same weight are compared, were performed on two batches of mice, in which a number of litters were equally represented and of which one was kept in the temperate room until 2 months old and the other in the hot room up to the same age. Other environmental conditions were identical. Immediately after being killed, their weight and length were recorded, the latter measured without stretching from the tip of the nose to the tail  
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end. The tail was measured from the anus. One of the ears was cut out and trimmed along the protruding fold. It was then pasted on a piece of millimeter paper and the area computed. Tail and feet were cut from the carcass and their total skin area determined. The skin of the body was carefully removed and the area computed. The sum of the area of the skin plus the area of the ears—multiplied by 4—plus the area of tail and feet was taken as representing the total body surface. The data were tabulated, for males and females separately, regarding body weight, total body surface, the constant in Meeh's surface formula, surface to weight coefficient, ear surface, ear surface in per cent of total surface, body length, length to weight ratio, tail length, and tail length in per cent of body length. There was a retardation of growth in the heat mice which averaged 4 gm. for males and 2 gm. for females.

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**Studies on the Adaptation of Albino Mice to an Artificially Produced Tropical Climate. III. Effect of the Tropical Climate on Growth and Pigmentation of Hair and the Dependence of these Integumental Functions on the Temperature Coefficient Law.**

*E. S. Sundstroem, Am. J. Physiol., 60:425, May 1, 1922.*

In connection with the measurements of the surface area of mice, the hair growth was compared in two series of a genetically homogenous mouse colony, one of which was kept at ordinary room temperature, the other transferred, when 3 weeks old, to a hot and humid environment. The mice were skinned at an age of 10 weeks and the hair removed with a safety razor. Mice which are suddenly transferred from a hot to a cool environment respond quickly to this change by a stimulated hair growth, but no change of hair growth was found in mice that for 2 months had been exposed to humid heat. The hair of recessive albino mice may, when exposed to humid heat or to the radiation of strong light acquire the power of producing pigment. In the beginning this is limited to individuals of a certain type, but may, in subsequent generations, extend to other individuals. It is suggested that the chemical processes that control the growth and the pigmentation of hair may possess different temperature coefficients. While cool climate seems more favorable to hair growth, the optimal temperature for pigment formation appears to fall within the range of tropical heat. The small amounts of color-producing enzyme that are supposed to be present in the skin of albinos may become active only in a climatic environment in which the skin temperature approaches the optimal temperature for the reaction of the enzyme.

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**Studies on the Adaptation of Albino Mice to an Artificially Produced Tropical Climate. IV. Effect of Light and Heat on the Resistance of Mice to Acetonitril.**

*E. S. Sundstroem, Am. J. Physiol., 60:434, May 1, 1922.*

In an earlier paper of this series it was shown that confinement of albino mice in humid heat retarded their growth. Since a retardation of general growth may result from hyperthyroidism, one must exclude the  
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possibility that the slow growth in the hot environment might be caused by the presence in the blood of excessive amounts of the thyroid hormone. To determine the activity of the thyroid in these animals their resistance to acetonitril was tested. Several litters of mice were divided into 4 batches, 1 male and 1 female group being kept at ordinary room temperature and the 2 remaining batches, males and females, were transferred to the hot room when 3 weeks old. When the mice were 3 months old the resistance tests were performed on the same day with freshly made dilution of acetonitril. A few days later the same procedure was repeated with 2 batches of male mice, derived from the same litters, which had been reared at normal room temperature, one in subdued light and the other exposed to the light from two 60 watt Mazda lamps at close range. The results show that the resistance of mice to acetonitril is not augmented in humid heat but is slightly diminished. Retardation of growth of mice in humid heat is therefore not attributable to a stimulation of the thyroid activity.

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**Studies on the Adaptation of Albino Mice to an Artificially Produced Tropical Climate. V. Effect of Humid Heat on the Blood Morphology of Mice.**

*E. S. Sundstroem, Am. J. Physiol., 60:443, May 1, 1922.*

These experiments sought to determine the changes which occurred in mice that for the greatest part of their life or since birth had been confined in humid heat. It was found that a progressive increase of the number of erythrocytes occurred in such mice, as compared to normal controls. Similarly a progressive diminution of the white count occurred in a number of generations of mice which were reared in humid heat. The observed increase of erythrocytes is referred primarily to inspissation of blood, while the diminution of the white cells was produced by high sensitivity to an increase of temperature exhibited by organs concerned in new formation of white blood cells.

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**Further Investigations on the Origin of Tumors in Mice. VII. Tumor Age and Tumor Incidence.**

*Leo Loeb, J. Cancer Res., 6: 197, July, 1921.*

Loeb describes the method by which the tumor age and tumor incidence is determined in certain family strains or groups of strains of mice, making possible a division into high, medium, or low tumor rate strains, and gives the total percentage of tumors in each of a large number of strains, as well as the percentage in each of 3 age groups in the same strain. He concludes that the tumor age and the tumor incidence of a certain strain are definitely determined by heredity, but that the tumor age may be a finer means of distinction between different strains than the tumor incidence. He finds that there is a definite relation between tumor rate and tumor age in mice. In those groups or strains in which the tumor incidence is great, the tumors tend to appear early, and in those groups or strains in which the tumor rate

is low, the tumors tend to appear late. When the mice are arranged in 3 groups of high, medium, and low tumor rate, the tumor age shows corresponding changes.

The period of life at which a certain kind of tumor shows a maximum frequency in a certain species is not definitely fixed, but varies with the rate of tumors in certain strains. The usual statistics represent an average between the maxima in different strains in which the maximum varies in accordance with the tumor rate. In addition to this general relation between tumor age and tumor rate, there is in certain strains a specific tumor age which may differ from that expected in the strain on the basis of its tumor rate; and in hybrid strains tumor rate and tumor age may be inherited independently of each other.

These relations between tumor age and tumor rate can best be explained, Loeb believes, on the assumption that the hereditarily transmitted constitution, so far as it represents the tendency of the organism to develop tumors, depends on the coöperation of multiple factors, which determine the intensity in the tendency to tumor development in a certain individual. In general, the greater the intensity, the earlier the tumors appear and the greater is the probability that in related individuals there exists likewise a tendency to the development of tumors. It is probable also that in addition to the general factors determining the intensity in the tendency towards the development of cancer, there exist factors which determine specifically the tumor age in certain individuals and strains.

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#### **The Fat of Adipose Tissue in Malignant Disease.**

*Archibald N. Currie, J. Path. & Bacteriol., 25:213, Edinburgh, April, 1922.*

Currie made a chemical investigation of the fatty tissues in cancerous patients and of any pigments that might be found in it and in cancerous tissue. The research was concerned more with the qualitative significance of the resting fat than with the fat transport to the liver. It was found that there was a constancy in iodin value of normal adipose tissue fat from any part of the body. Currie worked on 33 specimens of fat from postmortem and operated cases. Of these, 8 were from sarcomas (round-celled, spindle-celled), 21 from carcinomas, 2 from chronic inflammatory lesions, 2 from normal cases. Fat both vicinal and distant was taken.

From a table it can be seen that there is a progressive fall in iodin value from 74.4 to 60.8 (normal) and that unsaturation finds its highest expression in the fats adjacent to carcinoma, with sarcoma next in order. A fairly constant difference (average 4.5) exists between each successive average iodin value of the series. There is practically no difference between the iodin value of distant fat from a chronic inflammatory lesion, and that of normal fat. A degradation table is given which shows that the secondary fat in carcinoma is of the same degree of saturation as the primary (local) in sarcoma, the secondary in sarcoma holding the same relationship to the primary of its successor. In the human body in malignant disease there are 2 distinct manifestations of unsaturation activity, a local and a general one. The latter

would seem to be dependent on the former, and is probably due to the emigrant stimulus which gave rise to the high value in the primary. This is proved by the fact that there is a steady difference between primary and secondary which is maintained right through the degradation table. Very little is known of the molecular structure and chemical properties of the fat pigment, but it seems to play an important part in the mechanism of cell proliferation. Two experiments bear out the fact that the pigment acts as a protective agent as far as the preservation of its fat matrix is concerned. The results of these experiments show that the hydrogenation of the fat varies inversely with the degree of pigmentation, the pigment probably acting as a catalytic inhibitor, so that if the fat is highly pigmented and also highly unsaturated it exhibits a greater slowness in adjusting itself to corresponding body conditions than if the degree of pigmentation is lower. The variations in iodin value of the fat of adipose tissue in health and disease would suggest a localized enzyme complex as the cause of the change. Experiments on fat enzymes were carried out. The iodin values are showed in tables and curves. It can be seen by the curves that there is a constant and characteristic fluctuation in iodin value within the limits and conditions imposed, and the harmonic form of the curve is merely an expression of the change in the labile equilibrium of stimuli which independently produce saturation or unsaturation of the fat complex. In conclusion Currie states that the fat pigment seems to play an important rôle as far as the partial inhibition of reductase activity is concerned. It is an aid in preserving the saturation status quo of the fat molecule, preventing in some way the normal and counterbalancing effect of reductase against oxidase.

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**Cystic Xanthomas and the Genesis of Xanthomatous Tumors.**

*Eugen Kirch, Beitr. z. path. Anat., 70:75, Jena, Feb. 14, 1922.*

Although many studies on xanthomas have been published since Rayer first described (1835) this affection, no clear and uniform conception exists, particularly as to the genesis of the different varieties of these tumors and their differentiation from one another. However, there is a growing tendency to separate symptomatic xanthoma as it occurs in diabetes, icterus and nephroses, from the collective term "xanthomas," and to classify it in a special category as a lesion connected with disturbances of the cholesterol metabolism.

A second group includes the rather rare xanthomatous growths which occur in the form of tumors or nodes, developing to considerable size, and located mainly on the joint capsules, tendon sheaths, fascias and periosteum, i. e., starting from dense connective tissue. In the opinion of the majority of authors, this variety of xanthoma, described in France under the name of "myeloma or myeloid tumor," is a true neoplasm, a giant-cell xanthosarcoma. In contrast to this view, other investigators do not admit the blastomatous character of this formation, but regard it as reactive proliferations, as granulation tissue containing foreign body giant cells.

The author supports the theory of their neoplastic character. He  
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recounts two cases, a cystic tumor the size of a fist removed from the region of the knee in a man of 39 years, and an ovoid cystic growth (9.5 by 7 cm.) on the outer side of the left knee in a woman of 27. In both cases the diagnosis of xanthoma was confirmed by the appearance of the cut surface, marbled sulphur yellow and rusty brown, and the presence of doubly refracting fat. Both tumors consisted of an angiomatic portion and a sarcomatous part containing giant cells. There was a considerable increase in the cholesterolin of the blood in one of the patients.

Various tumors can develop into xanthomas, but a disturbance of the cholesterolin metabolism is the basis of this change; this disturbed metabolism does not cause the growth of a tumor, but the formation of xanthoma cells in a preexisting tumor. This does not solve the much debated question of blastomatous xanthomas. There is at present no explanation for the remarkable fact that the relatively rare sarcomas originating from dense connective tissue show such a marked tendency to xanthomatous changes.

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### Histogenesis of Transferable Chicken Leukosis. III. Lymphatic Leukosis.

*V. Ellermann, Folia Haematol., 27:171, Leipsic, Feb., 1922.*

In this disease the blood is normal, the liver is always enlarged and has white spots; the spleen is involved to a less degree; the kidneys show the same picture; the bone marrow is usually normal or may show occasional white spots; there is sometimes hyperplasia of the thymus, intestine and peritoneum. The hyperplastic tissue consists of medium and large lymphocytes; really lymphoblasts. The histogenesis of the splenic tissue indicates that they are neither myeloblasts nor erythrogones. In fresh cases it can be seen that the hyperplasia comes from the follicles while the pulp tissue is only pushed aside. The hyperplasia in the liver is in the periportal tissue and is very much like the picture of human leukosis. The hyperplasia in the kidney is often distributed in the form of flakes and the renal tubules are pushed aside by the newly formed tissue. The bone-marrow is usually normal, which argues for the lymphatic origin of the tissue. Occasional clumps of lymphocytes are sometimes seen. The same picture is seen in the thymus and intestinal mucosa. The greatest involvement is in the spleen; the follicles are enlarged to twice the normal size and consist of large lymphatic cells with many nuclear divisions.

Four cases are described in detail showing these changes. No changes in the blood were found. Three cases corresponded to the leukosarcomatosis of Sternberg, because they were characterized by large cells. It is not always possible to make a sharp distinction between lymphatic leukosis (small cell tissue) and leukosarcomatosis (large cell tissue with tendency to tumor formation). The large cell form is usually found in the chicken but there is not always a tendency to tumor growth.

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**Experimental Atherosclerosis of Aorta in Guinea-Pigs.**

*N. Anischkow, Beitr. z. path. Anat., etc., 70:265, Jena, March 11, 1922.*

To ascertain whether the aortic changes induced in rabbits can be produced in other animals, guinea-pigs were fed large amounts of cholesterolin, as contained in the yolk of  $\frac{1}{3}$ ,  $\frac{1}{2}$  and 1 hen's egg, diluted in 20-25 c.c. cow's milk. Of 17 animals only 7 supported the experiment without intestinal disturbance. Similar arte. 1 changes were constantly induced, and in all cases were preceded by the appearance of fatty substances on the inner parietal layers of the aorta; these substances were deposited in the capillary slits, between the endothelium and the internal elastic membrane. The process shows an infiltrative character and is termed lipoid impregnation. Later on, reactive phenomena of the aortic wall appear in the form of accumulations of ameoboid migratory cells, corresponding to the macrophagus cells (polyblasts) of granulation tissue. Simultaneously appear larger, transparent xanthoma cells, which should also be called macrophagous cells. From the median tunic of the aorta cells wander into the internal tunic which may belong exclusively to smooth muscle-fibers, or may be in part connective-tissue cells. Hyperplastic processes are not markedly developed in the elastic fibers, in comparison with analogous changes in the aorta of rabbits. In guinea-pigs, the powerful layer of fibrous connective tissue, with hyaline transformation, in the inner tunic, is wanting, as these changes are seen in human atherosclerosis. The experiments showed that lipoedemia or hypercholesterolemia alone is sufficient to induce the described changes in the aorta. For the production of aortic changes, as experiments with lanolin prove, it is not only the absolute amount of cholesterol introduced which is important, but also the form of the mixtures and combinations of cholesterolin. The changes in these cases show only quantitative differences from human atherosclerosis; there is no difference of principle. The idea of a fatty or lipoid degeneration of various elements of vascular walls in atherosclerosis, must be abandoned and replaced by the acceptance of a primary lipoid infiltration or lipoid impregnation of the vascular wall; that infiltration arises either in normal arterial wall, or in the arterial wall already predisposed by other influences. From this standpoint, the atherosclerosis must be considered not as a degenerative process, but more correctly as an infiltrative hyperplastic process.

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**The Water Content of the Tissues in Experimental Beriberi.**

*Dorothy Josephine Krause, Am. J. Physiol., 60:234, April 1, 1922.*

The object of this investigation was to ascertain whether there is an increase in the water content of the tissues in experimental beriberi. The author induced the disease in chickens and pigeons by feeding polished rice exclusively. Sand and water were also provided. Just before the last stage of the disease the animals were killed by decapitation and allowed to bleed dry. After preliminary treatment, the percentage of moisture was computed in brain, lungs, heart, liver,

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spleen, testicles, kidneys, pancreas, stomach, intestines, muscle and skin. The same procedure was followed with controls, the diet of which consisted of unpolished rice. Beriberi was also produced experimentally by the author in rats and guinea-pigs, and the moisture content of the organs determined. The tabulated results show that there is no definite increase in water content of the organs of beriberi chickens, except possibly in the skin. In beriberi pigeons there was observed an increased water content in the intestines, heart, lungs, skin, muscles and kidneys. Starvation, in proportion to the loss in weight in the beriberi birds, leads to a similar increase of water in these tissues. In the guinea-pigs which also showed scurvy, increased water content was not detected in determinations of separate organs, but when the animals were dried whole such a tendency was noted.

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**Histologic Changes in the Brain in Hyperkinetic Diseases of the Mouse after Diphtheria Infection.**

*F. H. Lewy, Klin. Wchnschr., 1:582, Berlin, March 18, 1922.*

On infection with living diphtheria bacilli the animals exhibit choreiform disturbances of the nature of mobile spasm. Great restlessness alternates with tonic rigidity. After diphtheria injection in mice the small neostriate cells of the brain are always affected, generally the central thalamus nucleus and in some cases the large-celled hypothalamic region. Depending on the severity of the infection, the change is a miliary necrosis without glia reaction, or a more chronic cell injury, which gives a picture similar to that of human chorea. In view of the author's earlier experiments with dioxid of manganese poisoning in rabbits, where only the large ganglion cells of the neoestriatum and paleostriatum were diseased, it would seem that certain toxins have a specific affinity, not only for certain areas in the brain, but even for special kinds of cells.

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**Experimental Study of the Kidney Changes in Diphtheria.**

*Erich K. Wolff, Klin. Wchnschr., 1:581, Berlin, March 18, 1922.*

The white mouse is better adapted to diphtheria experiments than the guinea-pig. Injection of living diphtheria bacilli produces typical fatal disease. The incubation and course of the disease are dependent to a high degree on the quality and quantity of the material injected; much less on individual factors. Typical pictures can be produced by the injection of living bacilli as well as by the injection of pure toxins. The typical diphtheria kidney is a dull, yellowish gray. The severest form shows total necrosis of the epithelium of the tubules with unchanged glomeruli and vessels. In mild forms, in addition to degeneration, there is replacement of epithelium and sometimes very violent regeneration with excessive division of nuclei and no involvement of the interstitial tissue and blood vessels, that is the picture of so-called nephrosis. In man, aside from mercury poisoning, diphtheria is the most frequent cause of acute nephrosis. Functional test of the kidney gives good results. The fact that the injury of the kidney is always combined with injury of the central nervous system, makes it probable that there is some permanent connection between them.

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**Macroscopic Findings on Corneas Exposed to Vaccine and Chicken-Pox Virus for Diagnostic Purposes.**

*Gino Calzavara, Igienè mod., 15:44, Genoa, Feb., 1922.*

In order to ascertain the virulence of vaccine virus, Paul advised that corneal inoculations and examinations of the macroscopic and microscopic lesions thus caused be made after fixation in bichlorid solution. The author has subjected Paul's method to a meticulous control and has effected a modification, according to which the animal is immobilized in a retention apparatus, the eyelids are kept open with a blepharostat, while scarifications at right angles or in irregular designs are made with needle and lancet. It is sufficient to let the vaccine drop on to the scarified cornea from a capillary tube held perpendicularly, with subsequent gentle massage. Calzavara has thus inoculated 17 different stocks of vaccine virus of various age, origin and activity; the result were that the inactive vaccines did not give the characteristic lesions when inoculated on rabbits' corneas; the weak vaccines gave a few small, isolated areas of ulcerative keratitis, frequently not crater-like; active vaccines gave numerous isolated areas of typical crater-like ulcerations, but confluent lesions could also be obtained if the scarifications have been too deep. The very virulent vaccines gave extensive lesions, confluent, with considerable loss of epithelial tissue, but insufficiently characteristic. Experiments were also made with the contents of a varicella pustule, inoculated on the cornea of a rabbit; the findings were similar to those obtained with inactive vaccines. Calzavara confirmed the excellence of the method of direct observation of the scarified and opaque corneas after bichlorid fixation according to Paul's method, both for purposes of differential diagnosis between lesions from vaccine and those of varicella and for determining the degree of activity of various vaccines. The diagnostic help offered by this method is immeasurable.

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**Histopathologic Changes Produced by Pfeiffer's Bacillus.**

*G. Santangelo, Ann. d'Igiene, 32:45, Rome, Jan., 1922.*

*Histopathology in guinea-pigs infected with Pfeiffer's bacillus.*—Brain: Diffuse vasodilatation; perivascular hemorrhages of the grey and white substances. Lungs: (first period) vascular hyperemia, subpleural hemorrhages, subpleural catarrhal broncho-alveolitis; (second period) vascular hyperemia, subpleural infarcts, diffusion of the subpleural catarrhal broncho-alveolitis to the central alveoli; (third period) acute confluent catarrhal broncho-alveolitis. Suprarenal capsules: diffuse vascular hyperemia; hemorrhages; fatty degeneration. Kidneys: vascular hyperemia; intertubular hemorrhages; turbid swelling of the epithelia of the tubules.

*Histopathology of pure influenza in man.*—Brain: diffuse vasodilatation; perivascular hemorrhages of the grey and white substances, most frequent in the centrum ovale; isolated hemorrhagic area. Lungs: (first period) vascular hyperemia, diffuse hemorrhages frequently localized to the subpleural alveoli, formation of infarcts, edematous zones; (second period) pneumonic exudative process combined with hemorrhages; (third period) multiple confluent diffuse lobular broncho-

pulmonitis. Suprarenal capsules: congestion and hemorrhages of the cortical and medullary substance; fatty degeneration. Kidneys: vascular hyperemia; intertubular hemorrhages; blood-casts; turbid swelling of the epithelia, especially of the contorted tubules.

The identity of the 2 histopathologic pictures is evident. The criteria suggested by this identity may be summarized under the following conclusions. With the subcutaneous introduction of Pfeiffer's bacillus alone, there may be reproduced most of the more important lesions found in cases of influenza that are without complications. It is therefore obvious that in man, too, the lesions above described should be attributed to the same microorganism, if that microorganism, investigated in time and by the proper technic, is found in the great majority of influenza cases. While it is recognized that the more typical lesions accompanying the disease are attributable to Pfeiffer's bacillus, it should be added that numerous other microorganisms, joining their action to that of the Pfeiffer variety, may heighten the seriousness of the disease and produce lesions of their own. In this way may be explained the frequent variations of the pictures described in medical literature as pictures of genuine influenza.

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**Experimental Pneumonia by Bacterial Symbiosis. The Pathogenesis of Influenza.**

*P. Caldarola, Ann. d'Igiene, 30:74, Rome, January, 1922.*

It is known that Pfeiffer's bacillus has a tendency to be associated with other pathogenic bacteria, both in the organism and in experimental and cultural processes. Caldarola has made an experimental study of the pathogenic mechanism of the infections associated with influenza and of the morbid phenomena and histopathologic lesions of this relation. In one series of 6 rabbits, there were administered subcutaneous injections with half a colony of Pfeiffer's bacillus and half a colony of streptococcus. Two more rabbits were used for control experiment, one of them inoculated with a whole cultural colony of Pfeiffer's bacillus, and the other with a whole cultural colony of streptococcus. Four of the 6 rabbits inoculated with the mixed culture died; the others, including the 2 used in the control, survived. These experiments show that, while the streptococcus is not pathogenic for rabbits, it is capable of producing in them a fatal septicemia when associated with Pfeiffer's bacillus. In a second group of experiments it was demonstrated that the streptococcus becomes pathogenic for rabbits even when Pfeiffer's bacillus is not mixed with the streptococcal culture but is instead inoculated in various parts of the body of the animal (pleural cavity and under the skin). It may therefore be deduced that it is not association pure and simple of Pfeiffer's bacillus with the streptococcus that makes general streptococcal infection possible in rabbits, but the decreased organic resistance of the animal due to the toxic action of Pfeiffer's bacillus, which acts as a true aggressor.

A study was also made of the morbid phenomena and the histopathologic lesions which Pfeiffer's bacillus, associated with other bacteria (pneumococcus, streptococcus), is capable of provoking when inoculated directly into the primary respiratory passages. These recall certain of the most typical complications of influenza in man: consider-

able hyperemia of the entire respiratory apparatus, desquamative catarrhal laryngotracheobronchitis, bronchopulmonary and peribronchitic foci. The entire condition was marked by the presence of numerous eosinophils and by large giant cells in hydropic and vacuolar degeneration.

On the basis of such results, it is possible to reconstruct the pathogenic mechanism of infections by bacterial symbiosis. The soluble toxins of Pfeiffer's bacillus, liberated by a leukocytic digestion, produce an imposing morbid phenomenology based upon congestive, hemorrhagic, and inflammatory conditions, with striking preference for the lymphatic glands and the lung. In the latter there appear interstitial hemorrhages, with spots, sometimes confluent, most obvious in the subpleural tissue, and sometimes so extensive as to occupy an entire lobe, more rarely the entire respiratory organ. Such a condition besides considerably reducing the defensive powers of the diseased organism, necessarily makes the affected organs more vulnerable, so that the bacteria naturally existing in the upper air passages (streptococci, pneumococci) may reach the bronchioles and alveoli and there give rise to phlogistic processes with characteristics peculiar to the complicating bacterial types.

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**Effect of Sunlight and Oven Heat on Experimental Tuberculosis.**

*J. B. Rogers, Am. Rev. Tuber., 6:119, April, 1922.*

A study was made to determine whether any increased resistance to tubercle bacillus infections could be obtained, either by sunlight or as the result of dry heat, and to learn the underlying cause for such resistance. Ninety guinea-pigs were infected with virulent tubercle bacilli, either by inhalation or subcutaneous inoculation. Thirty-four of the animals were exposed to natural sunlight daily, beginning with a five-minute exposure and gradually increasing to several hours each day during an average period of fifty-one days. Their average duration of life was forty-seven days. Twenty-seven of the pigs were exposed for five minutes to dry heat at a temperature ranging from 55° to 65° C., 20 of them twenty-four hours after inoculation and 7 of them three days after inoculation. Their average duration of life was forty-eight days. Twenty-nine of the guinea pigs were used as control animals. Their average life duration was forty-eight and a half days. The tuberculous involvement in these 3 groups of guinea-pigs was approximately the same. Sixteen white mice were inoculated intraperitoneally with 2 mg. of virulent bovine tubercle bacilli; 8 of them had been heated for five minutes three days before inoculation, at a temperature ranging from 55° to 65° C. The amount of tuberculous involvement was found to be approximately the same in the heated and nonheated mice. The conclusion drawn by the author is that natural sunlight and dry heat seem to have no effect on guinea-pigs or white mice inoculated with virulent tubercle bacilli. Results obtained in experimental infections of the guinea-pig do not necessarily demonstrate what might occur in man.

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**The Histology of Destructive Changes in Icteric Livers.**

*Emil Schwarz, J. Path. & Bacteriol., 25:207, Edinburgh, April, 1922.*

Many investigators have made extensive studies of the changes caused by icterus in the liver. The object of Schwarz's work was the examination of icteric livers with regard to certain histologic details in the destruction of liver cells, the meshwork of reticulum fibers, and the reconstruction of damaged trabeculas by various technical methods. Seven cases of grave mechanical icterus with destructive changes, caused by retention of bile, are described in detail. Schwarz verified the findings of other workers in the ruptures of the biliary capillaries produced by obstruction of the bile duct. As long as the thrombi formed only casts within the capillaries, the liver cells showed only slight degenerative metamorphoses. When the capillaries burst the thrombi are coiled up and part of the bile is diffused into the surrounding tissue. The thrombi are probably formed within the trabeculas when the latter are rapidly destroyed by polycholia combined with obliteration of the biliary ducts. Bile from the thrombi and the oval bile collections are given off into the surrounding tissue which is then imbibed with fluid bile producing a fine granular precipitate within the liver cells. Cell trabeculas containing thrombi are soon destroyed. Cell masses of this type usually appear as single rows instead of double rows forming the normal trabeculas. The portions destroyed by the larger clumps of bile with imbibition of the tissue following, usually show remnants of the pigment in the detritus cavities. The slow work of destruction allows for extensive regeneration in most cases and hinders any leukocytic infiltration and marked extravasation of blood. The regeneration did not appear as a rebuilding of whole trabeculas or acini, but as soon as a few cells are destroyed they are replaced by new ones. Schwarz did not observe any actual enclosure of biliary thrombi or clumps of bile within phagocytic cells, but whenever cells were attached to these formations or partially enclosed in the same they were apparently parts of destroyed portions of the liver parenchyma, such as liver cells or Kupffer's cells.

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**Hemosiderosis, with Reference to the Normal and Pathologic Histology of the Spleen.**

*Ulrich Strasser, Beitr. z. path. Anat., etc., 70:246, Jena, March 11, 1922.*

Siderosis is defined as an iron deposit of exogenous nature (from the food), and hemosiderosis as a hematogenous deposit of iron. By experiments on guinea-pigs on the chemical nature of hemosiderin it was found that in most cases hemosiderosis must be considered as due to iron oxd, and for that reason is analogous, in a chemical and histologic sense, to siderosis induced by iron oxid. If a higher decomposition product of hemoglobin containing iron and pigment could be deposited as a pathologic manifestation, this could be classed as hematosis. In this connection, Strasser alludes to the fact that with the

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Turnbull blue method, a greater quantity of iron can be demonstrated than with potassium ferrocyanid and hydrochloric acid. In Hellmuth's investigations on eclampsia an antithesis was shown, in that there was sometimes a bilirubin content of the serum and absence of hematin, and in other cases a minimal bilirubin content and much hematin. In the examination of rat spleens, there was found in the follicles a well-defined zone next to the zone of small lymphocytes; the former consisted of larger lymphocytes, less numerous, with clearer nuclei. Between them were red corpuscles and isolated elements with large nuclei, probably pulp cells. No sinus could be seen and pigment was absent, a condition which seems to be characteristic of this zone. The author proposes to name this the external follicular zone.

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**A Hitherto Unknown Iron Pigment in the Human Spleen.**

*Erik Johannes Kraus, Beitr. z. path. Anat., etc., 70:234, Jena, March 11, 1922.*

The author found accidentally in cicatrices of splenic infarcts a delicate green pigment, in addition to the common brown granules of hemosiderin. The spleen from a case of lymphatic leukemia offered opportunity for a more accurate investigation. This spleen contained peculiar, fibrous and intensely pigmented foci of the same peculiar pale greenish color. The finding of these fibrous pigmentary foci around the veins of the spleen leads the author to suppose that they represented organized hematomas. The pigment was formed by iron phosphate, pure and in loose combination. It seems that this pigment appears in the spleen only under certain pathologic conditions, namely when splenic tissue is destroyed by anemic necrosis.

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**The Stage of the Sublimate Kidney in Man, Based on Its Macroscopic and Microscopic Changes.**

*T. Nakata, Beitr. z. path. Anat., 70:282, Jena, March 11, 1922.*

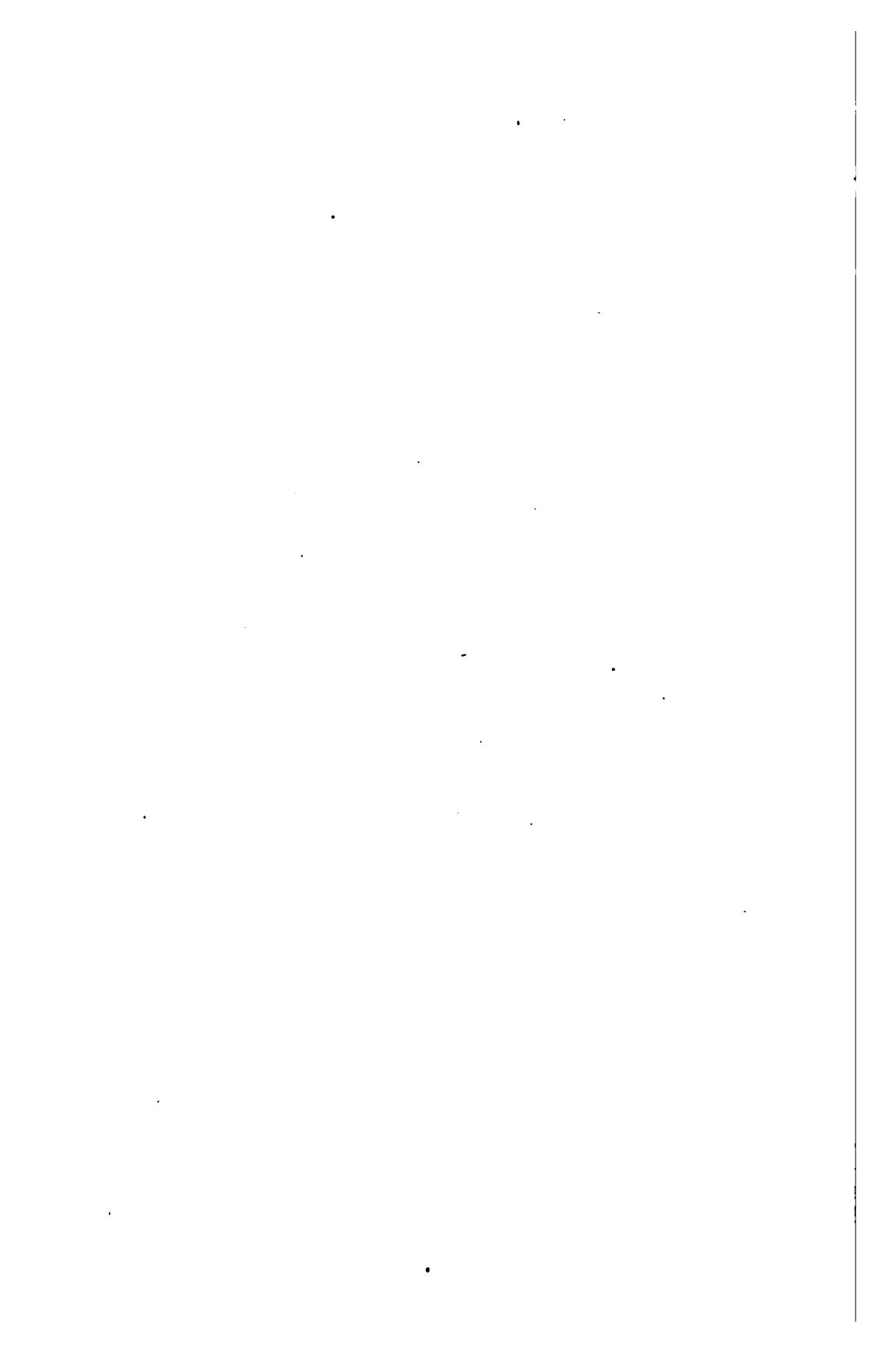
In regard to renal changes in intoxication by bichlorid of mercury the author reports his own observations of 15 cases of sublimate kidney in man and his experiments in rabbits. He distinguishes 3 stages in the course of nephritis induced by sublimate:

(1) *The short period of the red initial stage.*—In this stage the kidneys are distinctly enlarged in only a few cases; the capsule can be easily taken off; the consistency is soft; the superficies smooth, of a dark red or grey-red hue; the stellate veins are much congested; the surface of the section is abundantly impregnated with blood; the cortex is reddish or gray-red-yellow, and opaque; sometimes the glomeruli appear of a dark reddish color; the medullar substance is also reddish, occasionally more colored at the border, where in some instances it is dark red; the limit between cortex and medullar substance may be clear or indistinct. Histologically, we observe necrosis and desquamation of epithelium, chiefly in the convoluted tubules less in Henle's loop; no special changes in the glomeruli which are not enlarged.

(2) *The gray-white sublimate kidney.*—In this stage, the kidneys are enlarged, sometimes to a great extent and sometimes the increase is just recognizable; capsule can be easily peeled off; consistency soft; superficies smooth, and pale-gray or grayish-white in color, more seldom with a slight reddish hue, but not so red as in the following stage; in some instances the stellate veins are slightly congested or invisible. Surface of section: cortex grayish-white or whitish-gray, turbid, more rarely grayish-yellow or of a delicate pink hue; often swollen; the medullar substance in contradistinction to other forms of nephritis is pale—white-red or pink-white. The limit between the layers is sometimes indistinct, sometimes visible. Necrosis and desquamation of epithelium are more marked and more extensive than in first stage; on the fifth day processes of regeneration appear in the epithelium; the glomeruli are somewhat enlarged; in the interstitial tissue are foci of lymphocytes, plasma cells and isolated eosinophil cells.

(3) *The red sublimate kidney.*—In this stage, the kidneys are enlarged often markedly, sometimes less; capsule usually easy to peel off, but sometimes there are adhesions, chiefly in later cases; consistency soft, but in some instances without change; superficies smooth, more rarely spotted or granular; color reddish or red: Surface of section: cortex reddish or reddish-yellow, opaque, swollen; often certain areas show injection of blood sometimes in radial form. This is occasionally very marked in the pyramids. Medullar substances reddish or grayish-red, sometimes swollen. At that stage, the necrotic masses disappear. The epithelium is reproduced by regeneration; the cells in the interior of the convoluted tubules are often much calcified; those of Henle's loop less so.

The epithelial necrosis is produced by the action of the poison upon the renal epithelium. The calcareous deposit is of great value for the diagnosis of the sublimate kidney. The regeneration starts from the preserved epithelium of the convoluted tubules and continues in Henle's loop. As a rule, calcification appears at the end of the first week, only in exceptional cases it sets in two days earlier. Experiments on animals confirm the results obtained in man.



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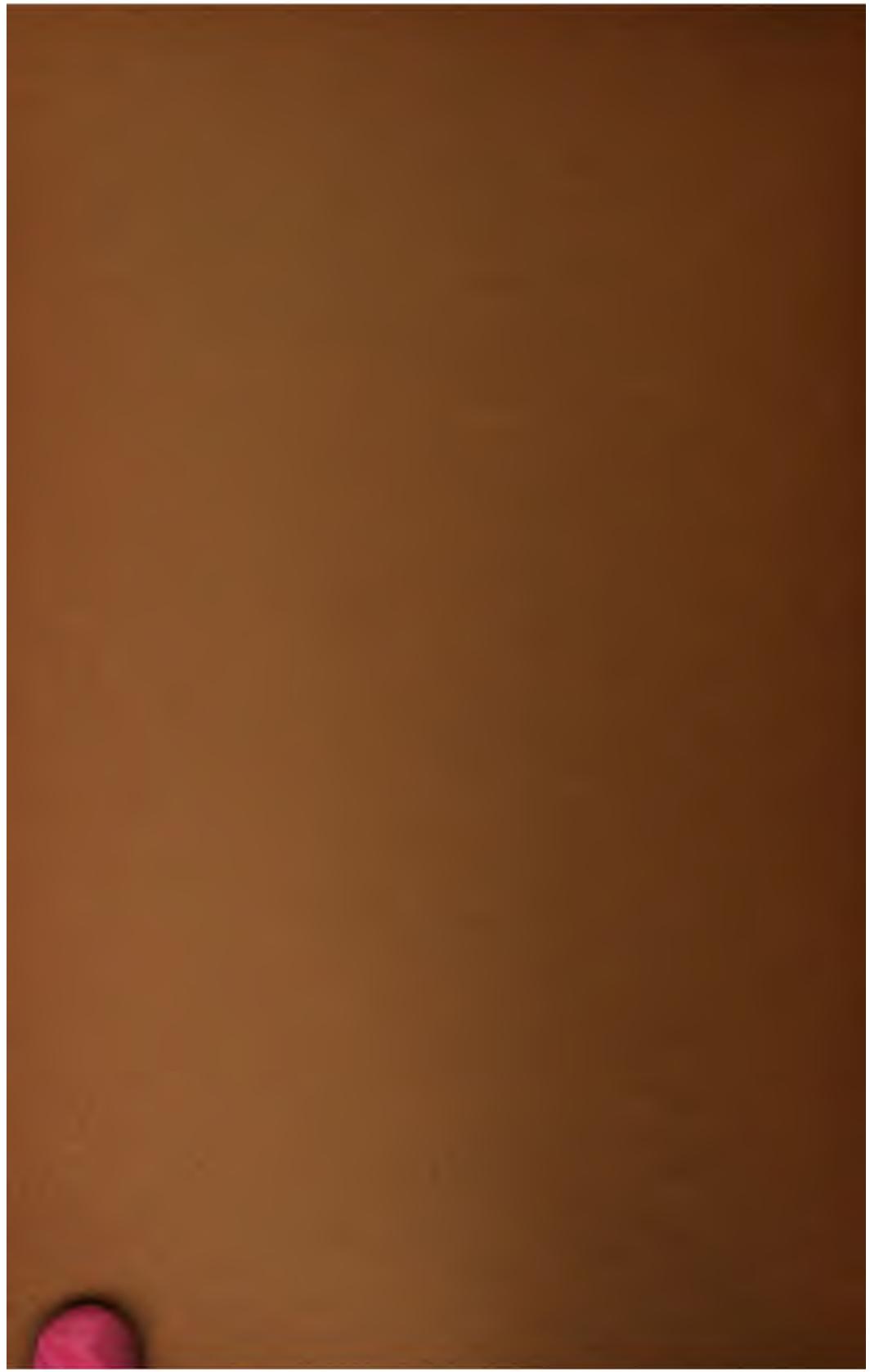
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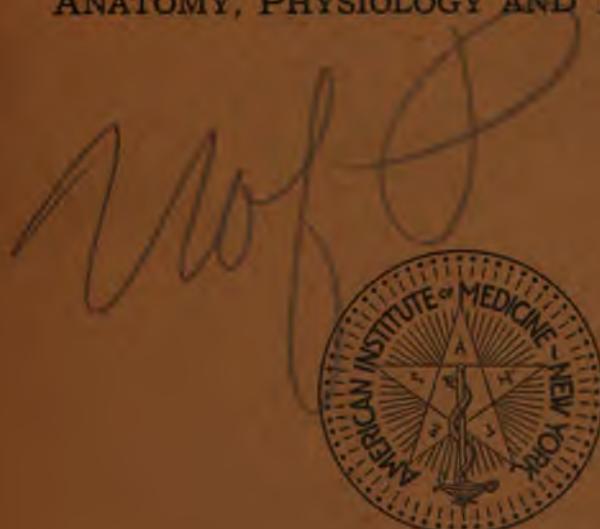
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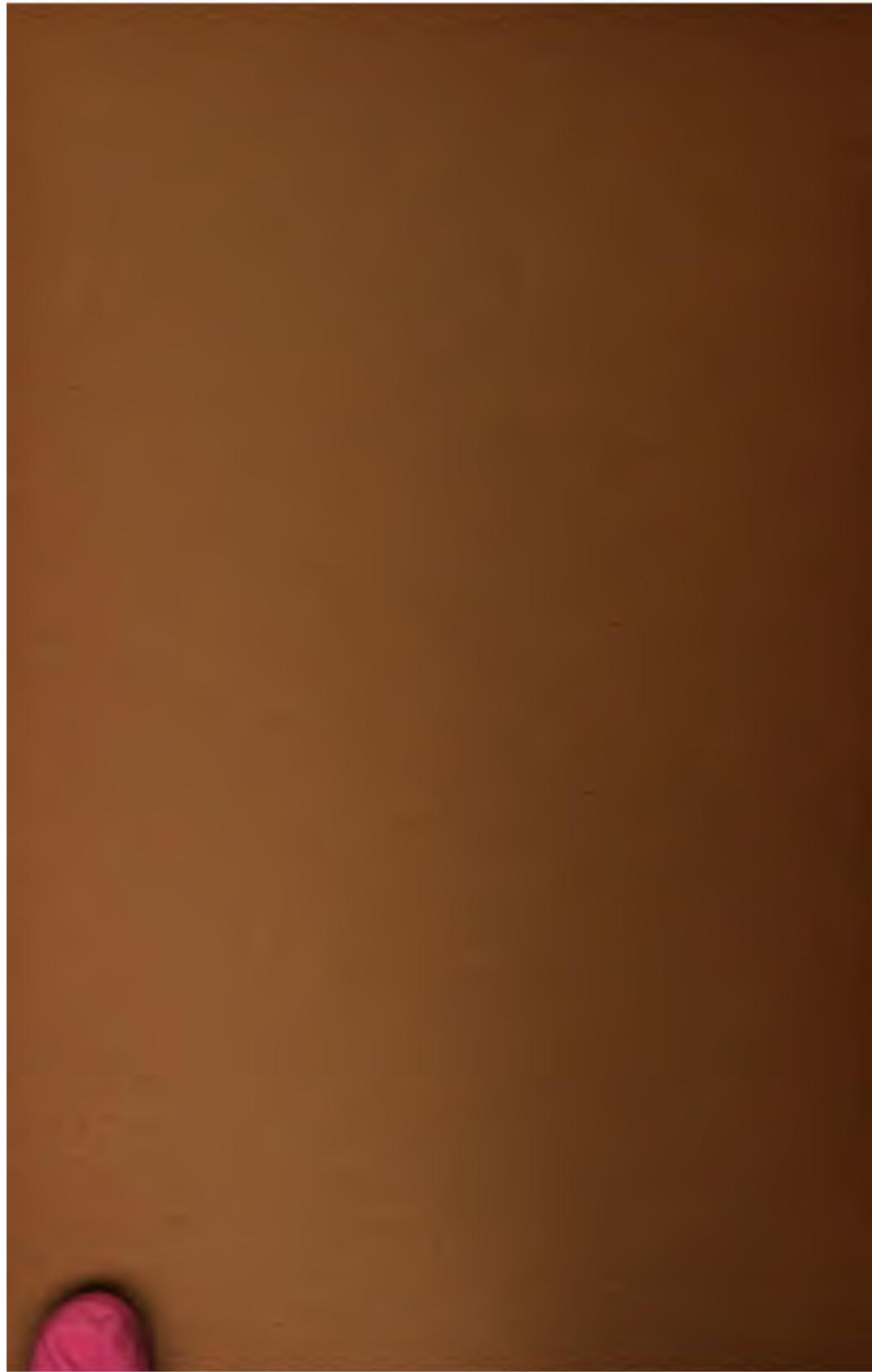
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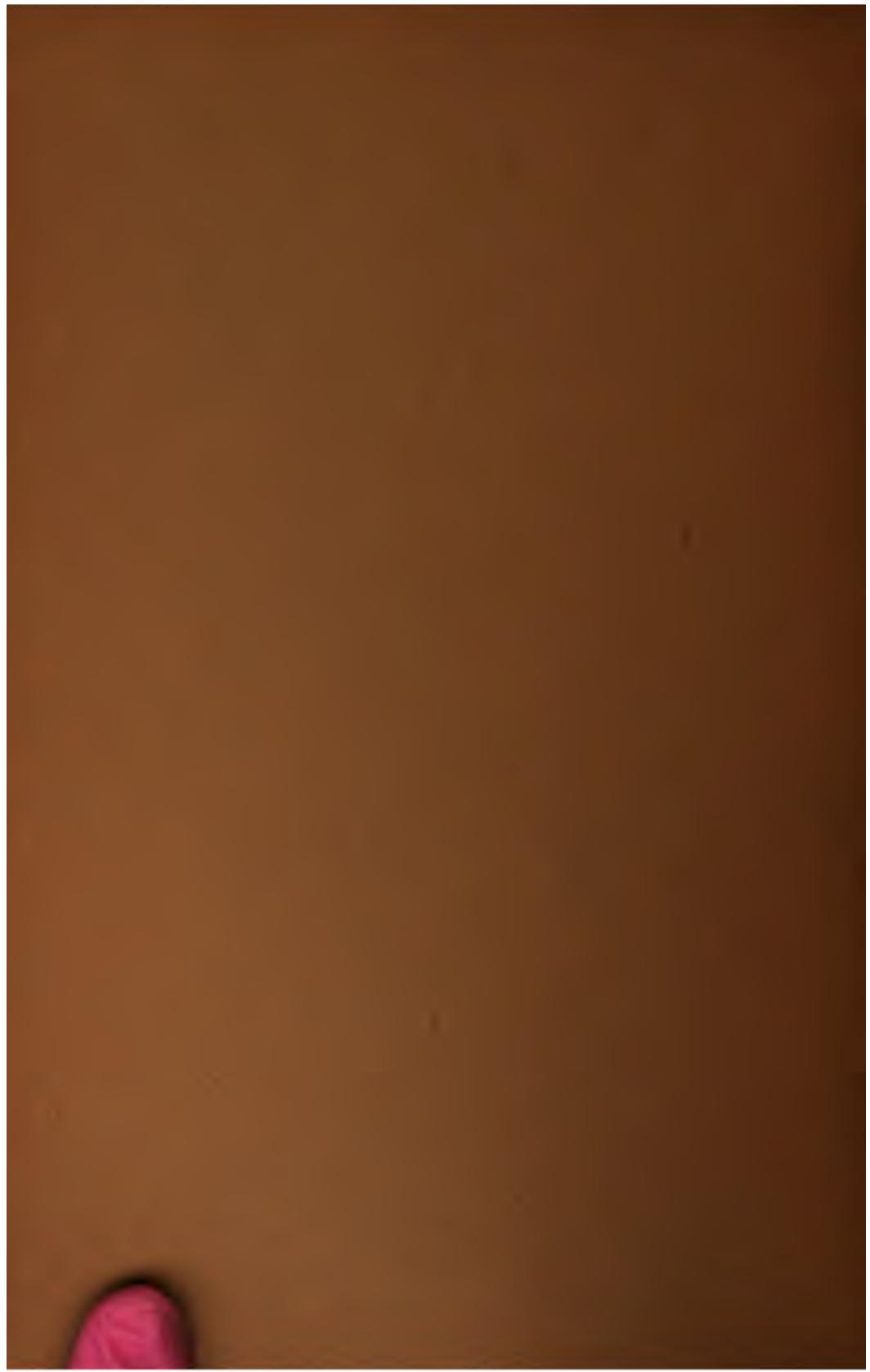
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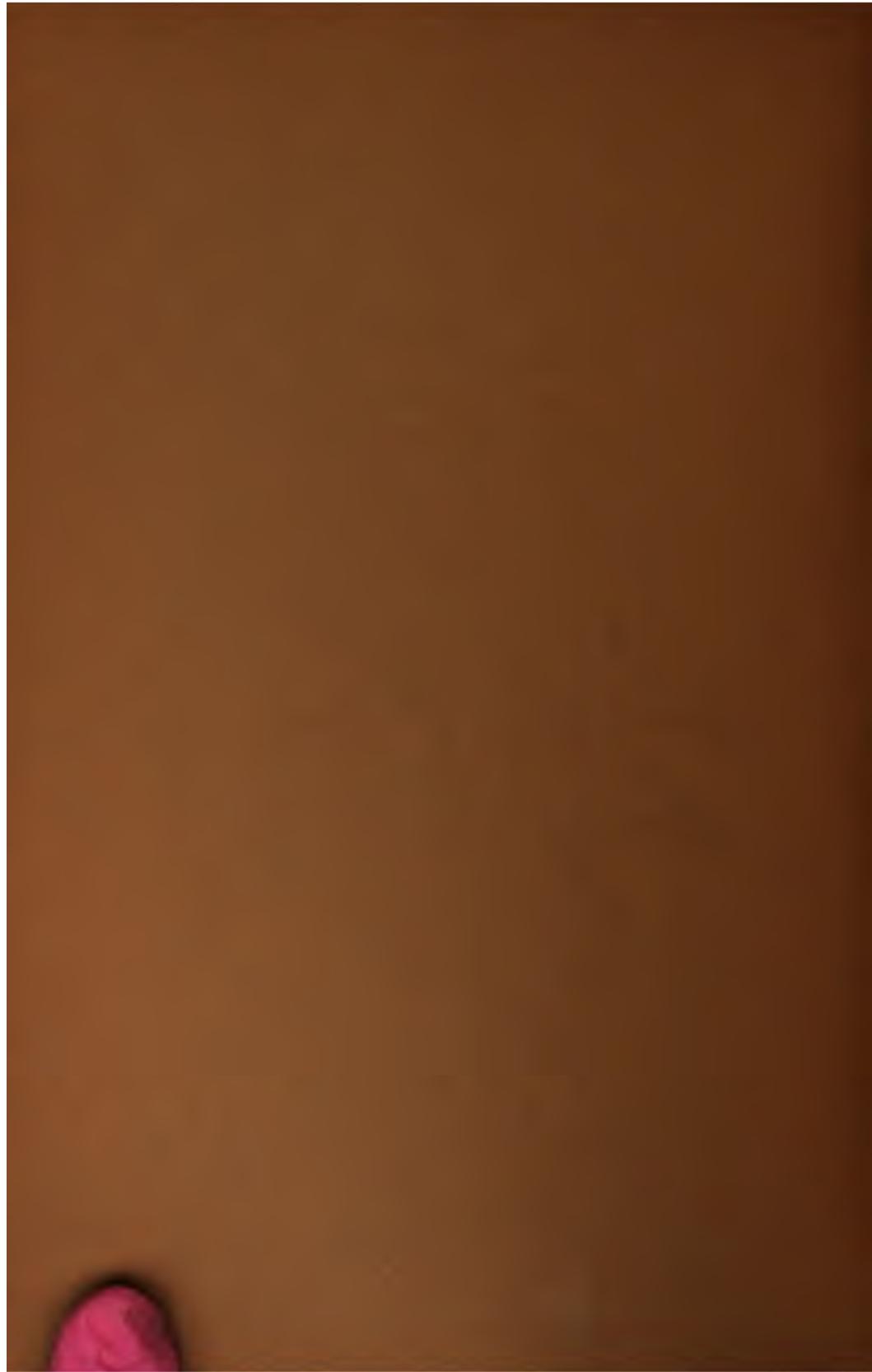
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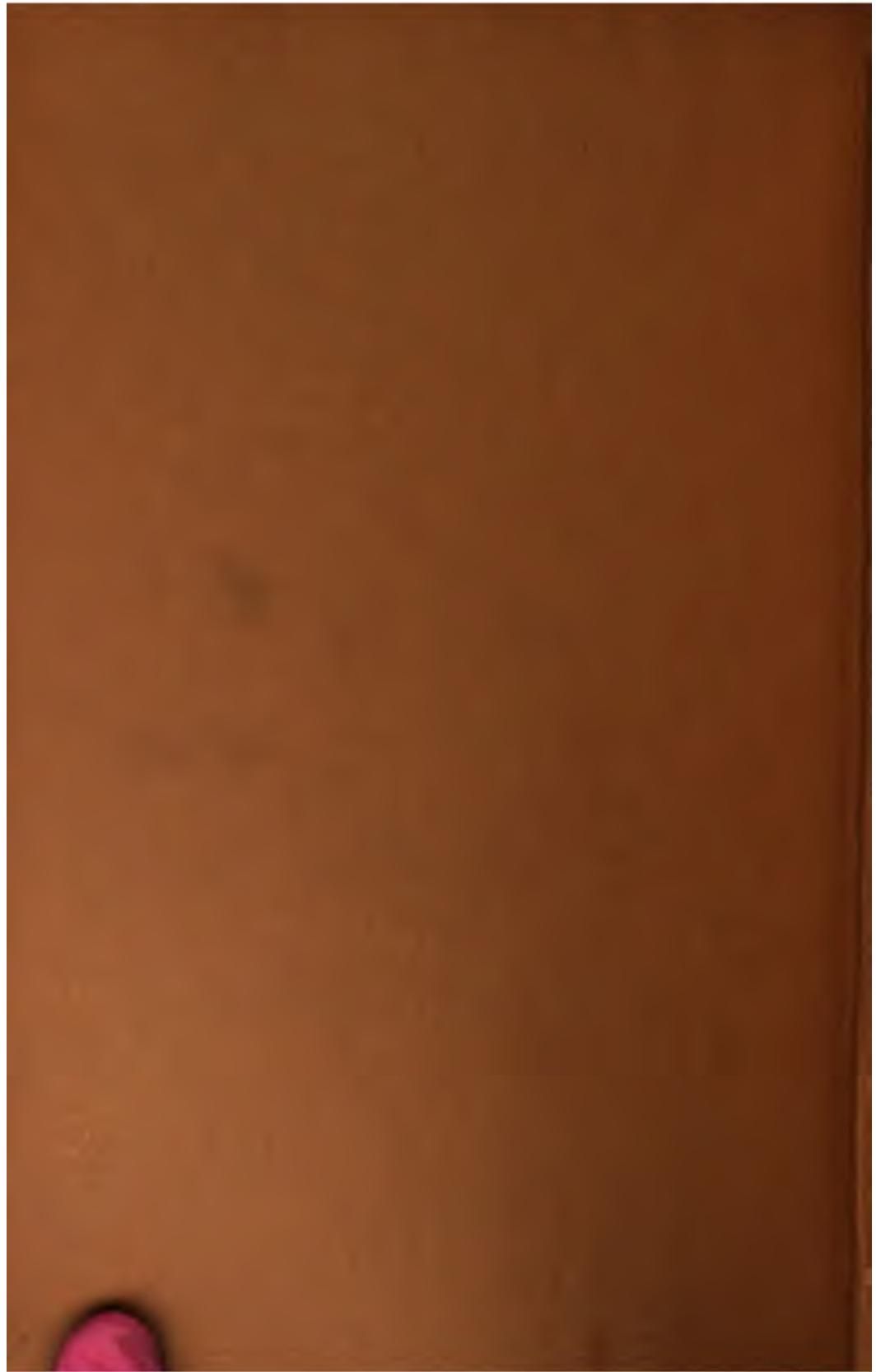


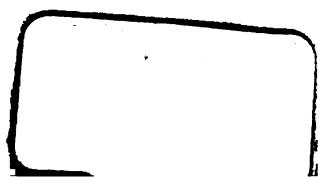














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